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STATUS REPORT

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DIET, NUTRITION AND CANCER PROGRAM
NATIONAL CANCER INSTITUTE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

Diet, Nutrition and Cancer Program

Status Report

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Public Health Service
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National Cancer Institute

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INTRODUCTION AND BACKGROUND

Results of numerous epidemiologic and laboratory studies have produced a growing awareness of the possible association between nutrition and cancer. However, the exact relationships between cancer, a disease of complex and uncertain etiology, and food and nutrition, a factor of multiple contaminants and components, remain to be determined. Some of the evidence linking diet and nutrition to cancer causation involves ingestion of substances that contain directly initiating carcinogens. Other evidence involves conditions that promote organ susceptibility and response to causative factors. In addition, nutritional support of the cancer patient clearly poses a spectrum of nutritional problems to the clinician. Treatment complications range from surgical trauma to radiation burns; medical complications range from acute sepsis to chemotherapy/nutrient interactions; and a variety of ethnic, sociological, and psychosocial complications occur in patients from infants to octogenarians.

Nutrition and nutrition-related research have been an important part of the National Cancer Institute's (NCI) activities for many years. The Diet, Nutrition and Cancer Program (DNCP) was established within the NCI to develop and disseminate information related to the role of diet and nutrition in the etiology and prevention of cancer and in the treatment, long-term management, and rehabilitation of the cancer patient. The DNCP coordinates NCI activities with those of non-NCI organizations and encompasses all phases of nutrition and cancer activities: research, education, training, resource development, and demonstration projects.

Nutrition research, as determined using the NIH definition, encompasses investigation of nutrient variables from the intact organism (including humans) to the cellular and subcellular level. It includes studies designed to assess both the consequences of food and nutrient intake and utilization and metabolic and behavioral mechanisms involved in feeding. This definition also includes the following:

- research designed to elucidate the metabolic role or function of nutrients in both animal models and humans;
- all studies concerned with genetic-nutrient-environmental interactions where a nutrient is a variable; and
- dietary studies expected to produce significant changes in health status, including the maintenance of health and the treatment of disease in humans. Such activities include clinical trials, epidemiological studies, metabolic studies, surveillance, and studies to monitor nutritional status.

ORGANIZATION AND APPROACH

Nutrition and nutrition-related research have been an integral part of NCI activities for many years. However, these efforts were officially designated a "program" in diet and nutrition with the passage of the 1974 amendments to the National Cancer Act. These amendments directed NCI to

> ". . . collect, analyze, and disseminate information useful in the prevention, diagnosis, and treatment of cancer . . . ."

From 1975 to 1978, the DNCP was administered by the Division of Cancer Cause and Prevention. In 1978, the program was reorganized and through FY80 was provided with central coordination through the Office of the Director, NCI. A proposed reorganization scheduled for early FY 1981 places responsibility for DNCP coordination within the Division of Resources, Centers and Community Activities (DRCCA). Although the program has historically been centrally coordinated, the actual direction of nutrition activities, including research, comes from the operating NCI divisions and offices. Each division retains responsibility for the programming, funding, and day-to-day management of specific nutrition projects. Representatives from the divisions serve on an Institute-wide working group to plan and coordinate program activities.

Guidance in program planning and conceptual review of program areas is the responsibility of the Advisory Committees or Boards of Scientific Counselors of each of the divisions or offices involved. Overall direction of the program is provided by the National Cancer Advisory Board.

The DNCP includes both extramural and intramural activities. The extramural projects are supported through grants and contracts. Research in etiology and prevention, cancer biology, treatment, and rehabilitation is managed by the Division of Cancer Cause and Prevention (DCCP), the Division of Cancer Biology and Diagnosis (DCBD), the Division of Cancer Treatment (DCT), and the Division of Resources, Centers and Community Activities. Research training and activities in resource development, communications, and central program coordination are managed by the DRCCA. Support services such as technical information, arrangements for meetings and workshops, and the services of a data coordinating center are provided by a contractor. Review of grant applications and contract proposals is performed by peer review groups in the NCI Division of Extramural Activities (DEA) and the NIH Division of Research Grants (DRG). Exhibit I presents the organization of the nutrition activities within the structure of NCI.

DNCP ACTIVITIES IN FISCAL YEARS 1979 AND 1980

As the DNCP enters its seventh year, program funding has shifted from directed contracts to investigator-initiated activities (grants). A program announcement for grants in diet and nutrition was published in September 1978. Grants in response to this were received in FY79. The DNCP also developed or participated in the issuance of several requests for grant applications, including nutrition and cancer rehabilitation and clinical nutrition research units. The program's support contract and one major treatment activity to study the support of patients with small-cell carcinoma of the lung were solicited through competitive procurement. In FY80 a contract was awarded to the National Academy of Sciences to develop an independent assessment of the relationship of diet to cancer incidence.

To stimulate interest in and expansion of research in cancer nutrition, the DNCP contacted over 20,000 people who were identified as having an interest in nutrition research. The availability of funds was announced in 32 major medical and nutrition journals, and young investigator awards were promoted to attract young people and new ideas. As a result of this effort, the number of grants funded in FY79 was increased 40 percent over the grants funded in FY78. This number was increased an additional 28 percent in FY80. The emphasis was on high-quality, investigator-initiated studies in all phases of diet, nutrition, and cancer.

An indication of the changing status of the DNCP during the past 2 years may be seen in the expansion of the program, represented by an increase in funding from an FY78 budget of $18 million to FY79 and FY80 budgets of $28 million, an increase of 56 percent. The overall budgets and allocation of funds are shown in exhibits II and III.

CANCER ETIOLOGY AND PREVENTION

The DNCP provides continuing support for epidemiologic studies to determine the underlying reasons for major differences in patterns of cancer incidence that characterize certain groups. Epidemiological and experimental studies are under way to determine whether dietary and environmental components serve as risk factors in the etiology of various site-specific cancers, particularly breast, stomach, and colon cancer. The possible etiologic role of fat, cholesterol, and lipids and the interrelationships between steroid hormone metabolism and breast cancer are currently being investigated. It is hoped that these studies will suggest new hypotheses for the etiology of breast cancer.

Other case-control studies are attempting to find relationships between dietary fiber and colon cancer etiology. It has been determined that the incidence rates for cancer of the colon and sex-linked cancers are lower among religiously active Mormons in Utah and California than

Exhibit 1
National Cancer Institute
Framework of Nutrition Research

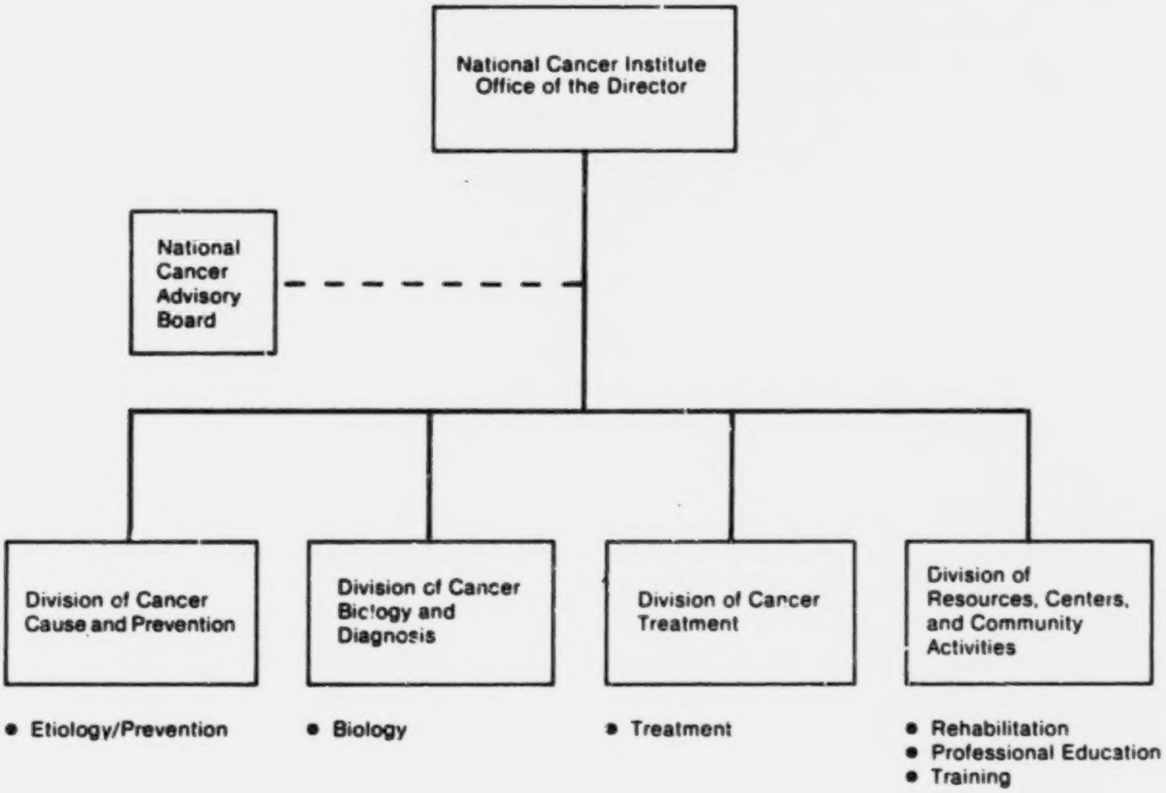
National Cancer Institute Office of the Director
National Cancer Advisory Board
Division of Cancer Cause and Prevention
Division of Cancer Biology and Diagnosis
Division of Cancer Treatment
Division of Resources, Centers, and Community Activities
• Etiology/Prevention
• Biology
• Treatment
• Rehabilitation
• Professional Education
• Training

Exhibit II
Diet, Nutrition and Cancer Program
FY 1979-1980 Obligations by Funding Mechanism
(Dollars in Thousands)

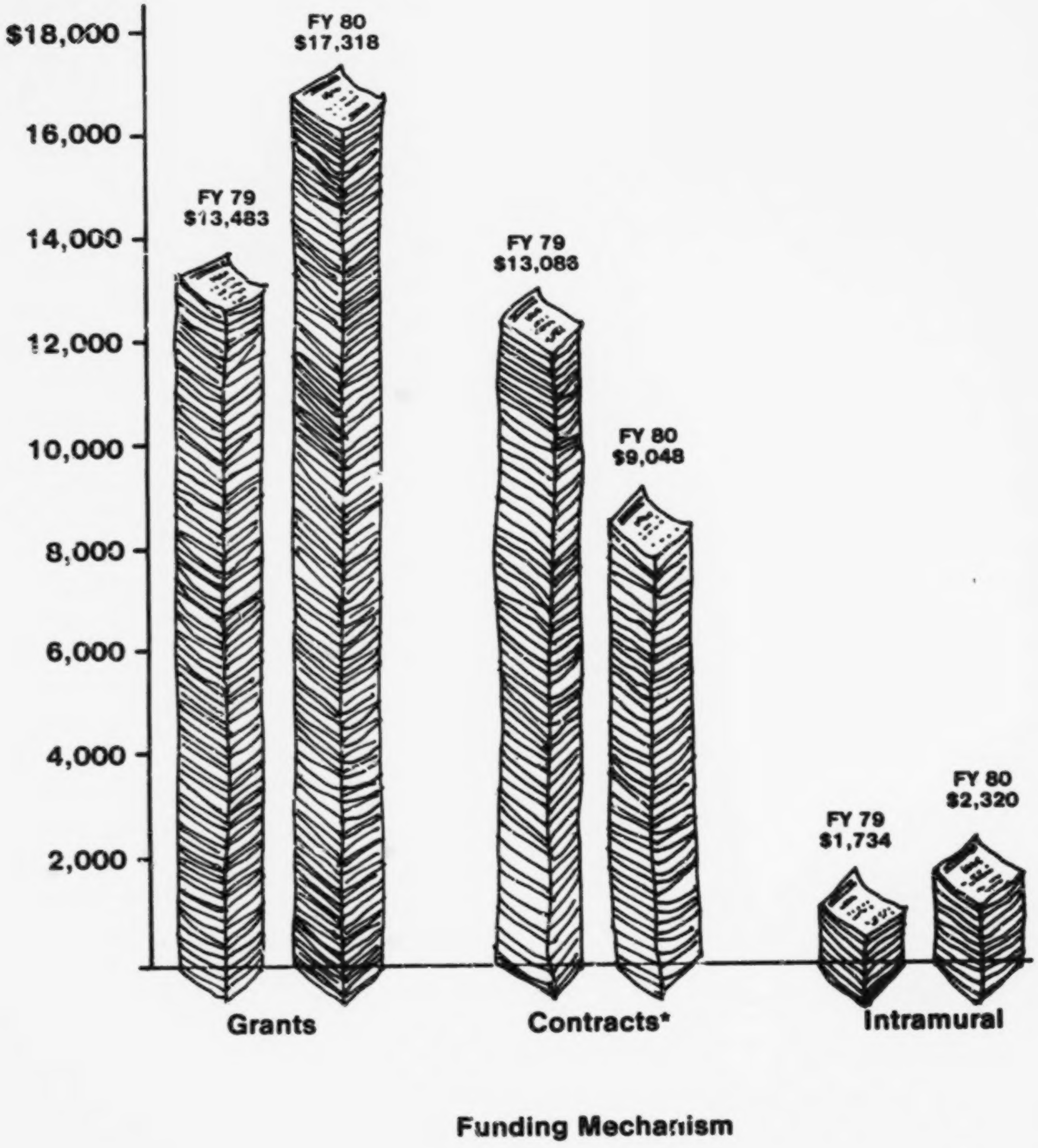

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Exhibit III
Diet, Nutrition and Cancer Program
Distribution of Nutrition Funding by Mechanism*
(FY 1979-1980 Obligations in Thousands of Dollars)

Mechanism	FY 79 Nutrition Funding	% of Nutrition Funding	FY 80 Nutrition Funding	% of Nutrition Funding	% Change
Grants	$13,483	47.6%	$17,319	60.4%	+28.4%
Contracts	13,086	46.2	9,048	31.5	−30.9
Intramural	1,734	6.1	2,320	8.1	+33.8
Total	**$28,303**	**100.0%**	**$28,687**	**100.0%**	**+1.4%**

*Percentages and dollar totals may not add due to rounding.

Exhibit IV
Diet, Nutrition and Cancer Program
Nutrition Funding by Award Type

FY 1979

Award Type	Number of Grants/Contracts	Total Award	Nutrition Award	Nutrition % of Total Award
R01	145	$ 10,066,324	$ 7,913,221	78.6%
R10	0	-0-	-0-	N/A
R13	1	34,990	4,199	12.0
R18	10	1,327,941	397,937	30.0
R23	1	32,750	32,750	100.0
R25	2	298,419	1,187	0.1
R26	29	2,211,537	1,704,989	77.1
P01	16	10,034,375	1,150,566	11.5
P30	27	25,821,339	1,911,981	7.4
Y01	5	5,366,966	782,047	14.6
N01	124	61,985,287	12,304,057	20.4
Z01	24	—*	1,733,600	—*
F32	3	45,834	45,834	100.0
K04	5	166,285	166,285	100.0
K06	1	25 000	25,000	100.0
K07	0	-0-	-0-	N/A
T32	4	830,966	129,373	15.5
Total	**397**	**$118,248,013**	**$28,303,026**	**23.9%**

FY 1980

Award Type	Number of Grants/Contracts	Total Award	Nutrition Award	Nutrition % of Total Award
R01	185	$11,919,299	$ 9,257,307	77.7%
R10	4	487,000	48,700	10.0
R13	2	77,374	38,687	50.0
R18	11	2,025,925	733,289	36.2
R23	1	32,750	32,750	100.0
R25	7	588,878	12,981	2.2
R26	31	1,912,179	1,872,075	97.9
P01	22	13,026,637	3,165,063	24.3
P30	26	29,900,560	1,703,428	5.7
Y01	7	3,974,690	890,857	22.4
N01	117	64,873,247	8,157,521	12.6
Z01	29	4,661,100	2,320,110	49.8
F32	0	-0-	-0-	N/A
K04	5	195,501	195,501	100.0
K06	1	31,626	31,626	100.0
K07	3	178,870	68,512	38.3
T32	4	1,087,721	158,270	14.6
Total	**455**	**$134,973,357**	**$28,686,667**	**21.3%**

***Figures for Total Award and Nutrition Percentage of Total Award not tabulated.**

the population at large, even in the same geographical area. Studies involving analysis of dietary and other lifestyle characteristics are in progress to determine the underlying reasons for their low risk of non-smoking-related cancer, especially of the colon. Research efforts are continuing to explain this. An association between colon cancer and dietary fiber intake is indicated by these epidemiologic studies.

A number of investigations sponsored by the DNCP are directed toward identifying individuals at risk to cancer, carcinogens in the food supply, and nutrients which may provide protection from the development of certain cancers. Education of health care professionals and the general public concerning the relationship between diet and disease is also of concern.

Another investigation is concerned with comparison of South African black males to both black and white males from the United States. The South Africans, with vegetarian dietary habits, are at low risk to prostate cancer, and excretion of urinary androgens and estrogens is lower than in high-risk nonvegetarian groups from the United States. Dietary manipulations are being employed to determine whether low-fat diets may diminish the risk of prostate cancer.

A newly initiated study addresses questions regarding the possible association of various dietary components with cancer of the breast and large bowel. This study takes advantage of an ongoing prospective study of risk factors for breast cancer in 121,000 nurses who complete a mail questionnaire on a biennial basis.

In addition to the ongoing observations of ethnic populations with differing dietary habits, studies investigating the role of lipid and cholesterol levels in mammary tumor formation in human and rodent populations are currently under way. The Breast Cancer Task Force of NCI has completed two studies on possible associations of dietary factors with breast cancer. These studies investigated ethnic populations with different dietary habits and different risks for breast cancer in Israel and in Hawaii and Japan. Three other task force studies are investigating lipid and cholesterol levels in relation to subsequent development of breast cancer (two studies) and cholesterol metabolism in breast cancer cases and controls. In addition to observations of obesity and weight loss in controlled dietary regimens in relation to the metabolism of estrogen and other steroid hormones, new information concerning the way in which diet affects the humoral and cellular immune response of both high and low tumor incidence strains of mice is being sought. Studies are being supported to compare the cocarcinogenic effects of polyunsaturated and unsaturated fats in an attempt to identify the type of fatty acid in a high-fat diet causing enhancement of mammary tumorigenesis.

Another area of investigation is the role of antioxidants in chemical carcinogenesis. In addition to continuing studies, new studies are under way to identify dietary factors that may retard cancer thought to be related to a high-fat diet. The efficacy of antioxidants such as BHT and BHA, as well as vitamin E and selenium, are being tested, and methods are being developed to determine the bioavailability of selenium in human subjects. DNCP also supports extensive research on other substances with anticancer properties, such as vitamin A and its analogs, vitamin C, vitamin B_6, and fiber.

Plausible theories regarding the relationship between diet and cancer are also being investigated. Individuals at high risk for breast cancer may have intestinal microflora that are efficient in producing estrogens or other substances that enter the circulation and serve as direct carcinogens or promoters of carcinogenic activity. It is postulated that specific diets may alter microbial populations which, in turn, enhance or diminish the risk for breast cancer.

When animals are permitted to self-select from several diets, the usual selection is that which maximizes growth rates but also enhances spontaneous tumor incidence. Another study will test the theory that undernourishment (not malnourishment) increases life spans, diminishes the incidence of cancer, and also prevents aging of the immunological systems. Studies are under way to evaluate mechanisms in rats by which long-term dietary restrictions diminish tumor incidence and to examine the possibility that physical exercise may produce the same effect.

Other studies are under way to detect proteins uniquely associated with the carcinogenic process. Evaluations of selected nutritional stresses such as amino acid deficiencies, protein deficiencies or high tryptophan diets in induction of liver cancer due to chemical carcinogenesis are also being financed by the DNCP.

The DNCP also supports research on specific substances known or suspected to be carcinogenic. Methods are being developed to detect, identify, and classify nitrosamines that may be found in meats, seafood, and fish meal under varying conditions. Conditions which contribute to the formation and occurrence of carcinogenic N-nitroso compounds or their precursors in various foods, including meat, cheese, milk, and dried egg products, are being studied. The influences of various methods of thermal processing (e.g., spray drying, drum drying, pasteurization, and cooking by frying, broiling, and microwave) are also being investigated.

The rainbow trout is being used to study the effect of dietary protein on hepatocellular carcinoma induced by aflatoxin B_1 (AFB_1). Exposure of trout eggs to AFB_1 for a short period yields a population of latent cancer-bearing animals in which dietary parameters can be evaluated.

The DNCP supports studies to examine interactions occurring between ethanol and the metabolic activation of chemical carcinogens. Increased risk of cancer (e.g., of the esophagus, colon, liver) in heavy consumers of ethanol is recognized as a significant health problem. Surface fluorescence of pyridene nucleotides as determined by optical techniques will enable researchers to study ethanol-carcinogen interactions and possibly identify molecular mechanisms by which ethanol may increase risk of cancer from chemical carcinogens.

Studies designed to examine the role of diet in the etiology of prostate cancer are also under way. Dietary intakes of fat, trace elements (zinc and cadmium), and vitamin A will be completed from histories and compared between cases and controls. Cadmium and zinc content of hair samples will be correlated with the data from histories.

Substances such as selenium, zinc, B-sitosterol, lithocholic acid, deoxycholic acid, and vitamin C are also being administered to colonic epithelial cells treated with organotropic carcinogens, alkylating agents, and antimetabolites to determine whether any modification of the acute reaction occurs and at which stage of the damage and repair cycle these dietary additions may operate.

The influence of dietary selenium on pancreatic carcinogenesis is being studied in Syrian golden hamsters. Investigations include the influence of excessively high and low dietary selenium on blood and tissue selenium concentrations, blood glutathione, and glutathione peroxidase activity. Requirements will be determined in the hamster based on growth, diet consumption, and selenium status. The aim of another study is to determine the influence of dietary fat types, individual fatty acids, and possible dietary fat and selenium interaction on development of spontaneous mammary tumors in mice. Current studies also focus on providing information about the role of saccharin in bladder cancer, evaluating the effect of diet and nutrition on cancer incidence among vegetarians, and delineating the characteristics of high-risk groups of cancer of the esophagus.

Epidemiological studies will continue to identify factors that promote or retard cancer. When a correlation is established, additional research will be undertaken.

The DNCP currently supports research on vitamin therapies in cancer patients and laboratory animals and epidemiological studies that correlate cancer incidence and vitamin levels in the diet. Roughly two-thirds of all research within this interest area is devoted to vitamin A and retinoid analog studies and development. Research labs have active contracts with the DCCP to synthesize retinoic acid and retinoid compounds similar to vitamin A for in vivo studies. These compounds will be used for other NCI antitumor studies and will be produced according to the specifications of the NCI Carcinogenesis Research Program.

The tumor-inhibiting effects of vitamin A and the retinoid analogs are being explored for several different organ sites, including breast, liver, oral, colon, epithelial, bladder, and trachea tissues. The epithelial studies include studies of bladder, mammary, and trachea carcinogenesis in the presence of vitamin A, effect of retinoids on the morphology and differentiation of epithelial cell membranes, and the use of topical carotenoid pigments inhibiting the formation of ultraviolet light-induced tumors.

One effort seeks to establish intake of vitamin A in women to determine a possible correlation with cervical cytology from Pap smears. These investigators are also searching for possible relationships between cervical dysplasia and retinoid receptor binding capacity in cervical tissue. Studies are under way to correlate the presence of vitamin A in the diet of Colombian citizens, Hawaiian ethnic groups, and Louisiana State residents, and the incidence of lung and other cancers among the survey sample. A similar study of diet and the incidence of colon and breast cancer in women is being done by an investigator at the Peter Bent Brigham Hospital via a mail questionnaire.

Other experimental studies of vitamin A include the use of hamsters to study the antitumor effects of vitamin A on two oral mucosal model systems, a study of vitamin A deficiency in the development of squamous cell carcinoma, and two continuing studies of retinoids in retarding the development of pancreatic tumors. In addition, several studies are specifically oriented to addressing retinoid dose-response and toxicity. One study is looking at the optimum time lag between carcinogenic induction in the mammary epithelial cells and the beginning of retinoid therapy. Other studies evaluate the effect of vitamin A on drug metabolism and the production of embryonic growth factor receptors on tumor cells.

There are several studies on vitamin E that use varying doses of vitamin E alone or in conjunction with selenium. One study looks at dietary vitamin E's effect on the tumorigenicity of established tumor cell lives. Another study uses chlorine and chlorinated compounds to evaluate the inhibitory effect of vitamin E and selenium on carcinogenesis in rats. Two additional grants are designed to study vitamin E as a reduced glutathione protector in liver cell tissue culture. Finally, the epidemiological survey in Colombia includes an assessment of vitamin E intake in the sample population.

Vitamin C intake is also being studied in the Colombian survey. Additional interest in vitamin C is found in studies of colonic epithelial cells and other organ sites. Vitamin C is used as a potential N-nitrosamine inhibitor in one carcinogenesis study and a methylcholanthrene-induced carcinogenesis inhibitor in another.

B-vitamin studies are another area of interest in cancer research. Several researchers are interested in the mechanism of vitamin B_{12} and folate uptake in lymphocyte and other mammalian cells. Another study at the University of Louisville is designed to investigate the possible use of a folate therapy to "rescue" normal cells from lethal doses of methotrexate in lymphoma-bearing mice. One vitamin B study looks at a novel vitamin B_6 metabolite peculiar to rat hepatomas and another uses pyridoxine-deficient mice to evaluate an enzymatic process in mice.

There is some research involving vitamin D, specifically a Tufts University study of familiar medullary carcinoma of the thyroid in which vitamin D plays a role in calcium metabolism. In addition, there are some general studies that look at the relationship of dietary vitamin uptake in the development of cancer. This includes a research program epidemiological project, a study that addresses antitumor components in specific food items, and a grant that includes varying the vitamin and carbohydrate content of laboratory animal diets in order to study the formation of urinary stones and the initiation of bladder cancer.

Two investigators, working cooperatively, have completed a review of the literature to compile a list of techniques for determining the mutagenic potential of various foods and body fluids/excretions of subjects consuming these foods. Recommendations for procedures of choice to be used in examining each of the sample types will be made after additional development and refinement procedures.

A contract was awarded to the National Academy of Sciences to develop an independent assessment of the possible relationship of dietary factors (nutrients, food additives, and contaminants) on human cancer incidence. A special committee on diet, nutrition and cancer will assess the state of the art, develop recommendations for the public, and develop suggestions for needed research to fill gap areas. The entire study will be completed in 3 years.

CANCER TREATMENT

Many cancer patients experience major nutritional problems. Anorexia (loss of appetite) and cachexia (a state of emaciation and malnutrition) frequently accompany the disease process and may be exacerbated by therapy. Anorexia is common in patients with a variety of cancers, varies with the type of carcinoma and the stage of the disease, and can occur early in the disease or as the malignant neoplasm spreads. Cachexia is particularly serious in the advanced cancer patient where decreased food intake combined with metabolic abnormality results in depletion of energy and wasting of body tissues. Malnourished patients may suffer impaired immune response, lose the capacity to counteract the complications of cancer, and become less able to withstand aggressive anticancer therapies. Preliminary clinical evidence indicates that an adequately nourished patient may have a better chance of undergoing successful treatment as well as being better able to withstand the rigors of the disease itself.

The seriousness of malnutrition in cancer treatment cannot be overstated; many patients die of no apparent cause other than cachexia. Development and application of methods for treatment and/or prevention of the anorexia, cachexia, and malnutrition syndromes in cancer patients are major goals of the DNCP. The Division of Cancer Treatment, which is responsible for aspects of the DNCP related to active oncologic therapy, has invited grant applications for clinical and preclinical research in the general areas of anorexia, cachexia metabolism, nutritional supplementation, and the nutritional complications of antineoplastic therapy. This element of the DNCP also includes research to develop improved formulations and delivery systems for nutritional support of cancer patients and research into the evaluation of alternative procedures for maintaining nutritional status, such as behavior modification and development of drugs to improve appetite.

A number of major investigations sponsored by the DNCP are directed toward evaluation of the efficacy of nutritional support procedures in preventing or treating malnutrition in cancer patients and development of improved formulations and delivery systems for nutritional support, including oral supplementation, total enteral nutrition, and total parenteral nutrition (TPN). Many chemotherapeutic agents now in use act as metabolic antagonists or blocking agents or create overt nutritional deficiencies. Research in progress is aimed at determining if nutritional support before or during cancer therapy can mitigate undesirable side effects, allow more intensive therapy to be given, or improve the quality of life of the patient. The effects of TPN in achieving total planned therapy, maintaining the immune response, and moderating the complications associated with cancer therapy are being studied, as well as the effect of TPN on tumor growth and host response to tumor.

In late FY79, a major new study was initiated which concentrates on small-cell anaplastic carcinoma of the lung (SCCL), in which weight loss, fatigue, anemia, and hypoproteinemia occur in various combinations and are aggravated by most chemotherapies. The objective of this study is to investigate the effect of TPN as an adjunct to chemotherapy and prophylactic irradiation in SCCL patients, on clinical response to treatment, treatment-related toxicity, and patient survival. Five institutions are participating in this study.

Eight institutions participated in a clinical study to examine optimal nutritional support as an adjunct to cancer therapy in the adult patient. The objectives were to determine the effects of TPN of the adult cancer patient on tumor growth, tolerance to antineoplastic therapy, and host/ tumor response, and to evaluate the efficacy of TPN in maintaining the nutritional status of cancer patients and improving the quality of life. Patient entry has been completed and the data collected are currently being analyzed.

A multidisciplinary project in pediatric cancer patients was designed as a pilot study to demonstrate that TPN used as an adjunct to cancer therapy is safe and effective in maintaining body weight and restoring malnourished cancer patients to nutritional adequacy. Here, again, patient entry has been completed and data are being analyzed.

The use of nutritional therapy in treatment of adults with malignant brain tumors was examined in a multi-institutional cooperative project. The objective of this study was to test the hypothesis that growth of brain tumors could be arrested by reducing blood levels of specific amino acids required by a particular tumor. This could be a very useful form of therapy to apply after surgical reduction of brain tumors.

The causes and effects of anorexia are the subject of a cooperative, multi-institutional research project to collect detailed dietary, nutritional, anthropometric, psychological, metabolic, and physiological data on a variety of cancer patients and controls. Data collection is designed to permit formulation of hypotheses on anorexia causes and interrelationships with cancer type, treatment modality, and associated phenomena. Other research in the etiology of anorexia focuses on particular aspects, such as learned food aversions, possible anorectic reactions resulting from radiation, chemotherapy, tumor-induced effects on the central mediation of feeding, and metabolism of particular substances.

INTRAMURAL RESEARCH

The intramural research program of the DNCP complements extramural efforts. Intramural research in cancer and nutrition is being done within the DCCP, the DCBD, and the DCT.

The bulk of the DCCP intramural research lies within the general category of skin cancer chemoprevention through the use of vitamin A. Several researchers are at present analyzing the morphological effects, biochemical mechanism, metabolic pathway, and dose toxicity of synthetic vitamin A (13-cis-retinoic acid) and its analogs in both cell cultures and laboratory animals. These studies should provide information on cellular and molecular basis of skin carcinogenesis as well as the therapeutic value of vitamin A before and after the onset of malignancy.

The Environmental Epidemiology Branch of the DCCP has several research projects under way that are evaluating the relationship between nutrition and cancer etiology. Several cross-cultural surveys and case-control studies are looking at the incidence of bladder, breast, colon, and other cancers with regard to dietary patterns among the target groups. Of particular interest in these studies is the consumption of nonnutritive sweeteners (saccharin), coffee, saturated fats, and drinking water. These projects are attempting to isolate nutritive factors in cancer etiology from other variations in lifestyle among the study groups. Another study within the DCCP is looking into the carcinogenicity of foodstuff contaminants and artificial sweeteners in primates. Two others address the effects of specific fatty acids and lipotropes in modifying the uptake and resistance to carcinogens in mammary and liver cells.

Basic research in energy exchange and expenditure is being conducted by DCBD. Laboratory studies on experimental animals involve the use of whole-animal, long-term calorimetry to investigate differences between normal and tumor-bearing animals and their response to TPN. Studies have been initiated to examine specific substrate metabolism, particularly of alanine and glucose. This laboratory also conducts physiological-behavioral research in animal models directed toward identifying the causes of the nutritional depletion and general deterioration of the host (cancer cachexia) with a view to blocking or reversing these systemic effects of cancer so that anticancer therapies can be more effectively applied.

The Surgery Branch of the DCT is actively engaged in assessment of the efficacy of TPN as a means of nutritional support for the cancer-bearing host. Studies are directed at conventional nitrogen balance and weight change with specific attention to muscle protein breakdown as assessed by 3-methylhistidine excretion in the urine. In addition, the first prospective randomized protocol for the use of TPN as an adjunct to radiation therapy and aggressive chemotherapy is in progress. This research includes prospective studies of the effect of TPN on the treatment of metastatic sarcomas in adolescents, diffuse histocytic lymphoma in adults, and patients with esophageal cancer.

In addition, this DCT intramural program maintains a large service component in which patients receiving TPN at NIH are studied for deficiencies of vitamins, trace metals (zinc, copper, chromium), essential fatty acids, and efficacy of TPN. Studies are done on gluconeogenesis, protein synthesis, glucose disposal, alanine kinetics, body content of potassium, mineral balance, and requirements for all known nutrients. The chief investigator also operates a laboratory which conducts studies in animal models and tissue-culture systems to investigate the adequacy of intravenous nutritional support, gluconeogenesis, glucose kinetics, gluconeogenic inhibition, and nutritional effects on wound healing in the cancer-bearing host.

Other intramural research in DCT involves a study of chemotherapy and oral antibiotics on gastrointestinal function. This particular protocol for lymphocytic leukemia patients may identify a biochemical basis for the nutritional depletion and general deterioration of the patients (cancer cachexia).

In FY80, the Environmental Epidemiology Branch of DCCP developed a number of studies to define the relationship between nutrition and cancer etiology. Some of these studies will explore changing patterns of colon cancer as populations in the U.S. migrate from the North to the South; others will combine metabolic determinations with epidemiology.

EDUCATION AND TRAINING

The DNCP placed a high priority on education in 1979 and 1980. A workshop on physician education held in FY79 drew attention to the need for incentives and educational opportunities for health professionals. Based on the recommendations of this workshop, NCI began to expand the clinical education grant program to include a separate nutrition component. The Institute also initiated a cooperative effort with the NIH Nutrition Coordinating Committee to support postdoctoral study in nutrition to augment the supply of qualified investigators. Several programs were set up to provide training in the broad areas of diet and nutrition research as these relate to cancer. Two programs, individual postdoctoral fellowships and institutional training grants, gave long-term support to promising individuals through the National Research Service Act. In addition, Cancer Research Career Development Awards were given to individuals entering a career in nutrition research.

The DNCP also supported efforts to assist cancer patients through nutrition education. Two handbooks for adult patients were identified in 1979 as being particularly useful: Health Through Nutrition, written by Ernest Rosenbaum and colleagues at the University of California, San Francisco; and Eating Hints: Recipes and Tips for Better Nutrition During Treatment, which was produced at the Yale Comprehensive Cancer Center. Eating Hints provides recipes and helpful suggestions for coping with major nutritional problems such as nausea, vomiting, and mouth sores which cancer patients frequently confront. A third handbook, Diet and Nutrition: A Resource for Parents of Children with Cancer, was developed by NCI and the Candlelighters. In the first 6 months after the announcement of publication, 274,000 copies of Eating Hints and 35,000 copies of Diet and Nutrition were requested and distributed. Efforts are under way to make the publications more widely available.

RESOURCE DEVELOPMENT

A vital issue which the DNCP addressed in 1979 was the design and standardization of techniques in nutritional assessment. Preliminary evaluations of the techniques studied were completed early in 1980.

In FY79, the DNCP, through DCT, supported 10 studies to develop or improve techniques for assessing nutritional status and determining nutritional requirements in cancer patients. Tools being developed for nutritional status assessment include the use of computerized axial tomography to measure fat and muscle compartments, portable ultrasound devices for measuring muscle and adipose tissue thickness, specially designed stereometric sensors for recording the body form as a three-dimensional optical mode which can be analyzed by computer, prompt gamma-neutron activation techniques to measure total body nitrogen in vivo, and whole-body impedance measures as estimates of total body water and extracellular fluid volume. Other studies involve defining existing techniques and procedures that can be used to measure body composition changes in cancer patients and the effectiveness of nutritional support in ameliorating these alterations. Core data on anthropometric, biochemical, and clinical parameters are used to test, validate, and standardize these new and existing techniques. Early in 1980 these techniques were evaluated and those which showed promise were funded for an additional year.

The DNCP coordinator serves as NCI's representative on the NIH Nutrition Coordinating Committee. While many of the NIH Institutes support nutrition research, four Institutes, NIAMDD (now NIADDK), NHLBI, NICHD, and NCI, provide major support to nutrition research.

To expand its program activities, in January 1979 the DNCP collaborated with the NIAMDD and the National Institute on Aging (NIA) in issuing invitations for applications for core grants in support of clinical nutrition research units (CNRU's). These grants facilitate the planning and coordination of an integrated array of research, educational, and service activities oriented toward human nutrition utilizing the facilities and staff of the CNRU on a shared basis. One such unit was funded in FY79 and two were funded in FY80. These will provide core support to allow institutions to bring together groups involved in nutrition-related research and to recruit people from other disciplines. An integral part of the program will be the education of medical students, house staff, community physicians, and other health professionals. These units will extend nutrition education for health professionals and provide expert nutrition consultation services in their regions of the country.

NIADDK and NCI are developing a joint management system for the CNRU's and are instituting a series of meetings with CNRU directors, the first of which was held in December 1980. One of the major objectives of the meeting to begin a discussion of new ways to stimulate interdisciplinary nutrition research.

The NCI also participated in two trans-NIH training program announcements for institutional training grants and postdoctoral fellowships, published in September 1979. Thus far these announcements have had little effect on the NCI grant program in research training. Only one training grant application was received and that application was not approved.

The DNCP continues to support a comprehensive Nutrient Data Base/Scientific Dietary Analysis System that is used in analyzing the nutritional composition of individual diets. This system, which is computerized, utilizes a coding manual to facilitate quick and accurate preparation of food-intake records for analysis.

WORKSHOPS AND CONFERENCES

In addition to support for research projects, topics of special interest were addressed in conferences and workshops.

Research Directions for the 1980's

During FY79, a workshop was held to identify and develop a responsible set of research directives for the 1980's in enteral and parenteral nutritional support of the sick and malnourished patient. Malnutrition in the cancer patient is recognized as a serious clinical problem contributing to both morbidity and mortality. The prospects for improved nutrition and the efficacy of such treatment through parenteral and enteral nutritional support on patient survival and quality of life are important areas of ongoing research. A panel of scientists and clinicians stressed the need for reliable assessment parameters of nutritional status in order to measure accurately patient response to nutritional support treatment. Basic research is also needed to examine in vitro the specific nutritional requirements of tumor growth with the aim of identifying nutritional support systems that favor host over tumor. Participants in the workshop agreed that nutritional rehabilitation after successful oncological therapy merits continued study.

The proceedings of this workshop were published in the American Journal of Clinical Nutrition, Vol. 34:6, 1981.

Physician Education

The DNCP continued to campaign actively for increased emphasis on nutrition education in medical training and practice. A workshop was held on physician education in cancer nutrition. This explored curriculum needs, available educational materials, and opportunities and incentives for the medical practitioner in cancer nutrition.

Recommendations from this workshop included assistance in the development of teaching and audiovisual aids in nutrition and validation of educational evaluation mechanisms. These will help to guide planning in nutrition education initiatives in FY80. During FY79, NCI, together with other NIH Institutes, provided additional training grants to support postdoctoral study in nutrition and cancer, in particular.

The DNCP plans to encourage inclusion of nutrition in the curricula of primary and secondary schools as well as of universities. Workshop participants identified a need for appropriate educational materials for students at all levels of instruction in nutrition. Development of these resources, including audiovisual aids, was undertaken in 1980.

Recommendations and reports from this workshop were published in Nutrition and Cancer, Vol. 2:1, 1980.

Alcohol and Cancer

A Workshop on Alcohol and Cancer was sponsored jointly by the Division of Cancer Control and Rehabilitation and the Division of Extramural Research of the National Institute on Alcohol Abuse and Alcoholism. The purpose of this conference was to present evidence that might better define the scientific basis for an interrelationship between alcohol and cancer. Concomitantly, workshop participants sought to identify gaps in knowledge and to recommend future areas of study and investigation.

Alcohol combined with tobacco smoking is an established risk factor for cancers of the oropharynx, esophagus, and larynx. An association between alcohol consumption and primary-level cancer exists, but probably involves less direct action. The DNCP is encouraging research, especially investigator-initiated studies, in the broad areas of epidemiological studies in alcohol-related cancer and basic research on alcohol effects on carcinogenesis. Promising areas for future investigation include case-control studies to clarify the process by which alcohol promotes cancer, the mitigating effects of tobacco, dose-response relationships, and nutritional cofactors. In addition, basic research in etiology should include the importance of the presence of low levels of carcinogens in certain fermented and distilled beverages (e.g., nitrosamines), the effect of nutritional deficiencies commonly associated with alcoholism on cancer development, induction by ethanol of microsomal enzyme activity involved in carcinogen metabolism, and contact-related effects of alcohol consumption on the development of cancer in the upper gastrointestinal tract.

The proceedings of this workshop were published during 1979 in Cancer Research, Vol. 39:2815-2908.

In FY80 four conferences and workshops were sponsored by the DNCP.

Esophageal and Prostatic Cancer in Blacks and Whites

In October of 1979 a workshop on Esophageal and Prostatic Cancer in Blacks and Whites was jointly sponsored by the DNCP and the American Health Foundation. The purpose of this workshop was to investigate the differences in the rates of cancer of the esophagus and prostate in blacks and whites. The participants' goal was to determine the accuracy of the reported rates and to assess the degree to which the rates reflect real differences between the races. Recommendations for future research emphasized the need for an interdisciplinary approach to the issue. Reports from this workshop were published in Preventive Medicine, Vol. 9:587, 1980.

Fat and Cancer Workshop

The causal relationship between dietary intake of animal fat and cancer was the topic for discussion at the Fat and Cancer Workshop held in December 1979. Workshop participants shared research findings and objectives concerning the relationships between lipid metabolites, intestinal flora and colon cancer; acids, steroids and cancer; lipids and the immune system; and hormones, fat, and cancer.

Recommendations from this workshop included: (1) develop new markers of dietary ingestion to characterize intake of various vitamin trace metals and fats; (2) standardize experimental protocol and dietary fiber sources for comparative studies; (3) investigate the effects of infection or obesity in immune responsivity and carcinogenesis; and

(4) design studies to investigate the effects of dietary factors in the various stages of tumor induction and promotion to determine the stage at which a dietary manipulation is effective.

Proceedings of this workshop will be published in Cancer Research.

Nutrition of the Cancer Patient

In January 1980 the DNCP sponsored a workshop on the Nutrition of the Cancer Patient. The current states of knowledge in the area of anorexia, host/tumor metabolism, and nutritional support were reviewed as they pertain to basic and practicing clinicians. It was generally concluded that replenishing the metabolic deficiencies of the cancer patient is not a simple process. Failure of replenishment may be related to altered host metabolism, which is only partially understood. Failure may also occur because the nutrients delivered do not have the optimal composition, the route and schedule of delivery are not optimal, the duration of therapy is not sufficient, and/or the timing relative to the treatment aimed at ablating the cancer is not optimal. Further research aimed at these issues was encouraged.

Proceedings of this workshop will be published in Cancer Treatment Reports.

Selenium, Vitamin E, Lipid Oxidation and Carcinogenesis

A workshop on Selenium, Vitamin E, Lipid Oxidation and Carcinogenesis was also held during FY80. This workshop explored current knowledge regarding the relationship of selenium, vitamin E, and lipid oxidation to cancer; panels of scientists and clinicians identified future study area of study and investigation.

Proceedings will be published in the Journal of the National Cancer Institute.

LIAISON

Effective liaison with individuals and groups interested in diet, nutrition, and cancer research is essential to the success of the DNCP. It is also critical to the fulfillment of DNCP's mandate to disseminate information on diet, nutrition and cancer. This effort was continued and extended throughout FY79 and FY80.

The NIH Nutrition Coordinating Committee (NCC) provides coordination for the activities in diet and nutrition for all Institutes of the National Institutes of Health and other agencies within the Department of Health and Human Services. The coordinator of the DNCP is a member of the NCC. The DNCP participated with the NCC in issuance of the RFA on clinical nutrition research units. The conference on Research Directions for the 1980's supported by NCI was a joint effort of the NCC and other Institutes. A conference on the Assessment of Nutritional Status is planned for FY81.

Among those interested in nutrition and cancer research are other government agencies, professional societies, Congress, public health groups, private organizations, industry groups, scientists, physicians, other health care professionals, and cancer patients and their families. The DNCP attempts to coordinate program activities with as many of these groups as possible and to maintain active channels of communication with each. This is accomplished through the use of consultants; sponsorship of workshops and symposia, or participation in them; ongoing review of journals, proceedings of scientific and medical conferences, and other professional publications; issuance of program announcements, reports, and other documents; and joint planning with other governmental and nongovernmental groups.

FUTURE PLANS

The DNCP plans further expansion of its activities. The budget in FY81 is expected to be $28.4 million. The trend toward grant-supported research in nutrition will continue, and the internal NCI coordination of the DNCP will be strengthened.

NIH is considering the initiation of a public education program for nutrition in conjunction with supermarkets. Evaluation of one such study carried out by NHLBI and Giant Food, Inc., indicated an increase in consumer awareness of health-related nutrition issues as well as changes in buying patterns. The NIH expanded program would include several Institutes and would involve monthly or semimonthly educational programs focusing on supermarkets. NCI would sponsor one of the programs during the first year of the study.

Program planning will focus on increasing capabilities for diet, nutrition and cancer research. In an effort to foster interdisciplinary cooperation between scientists expert in nutrition and oncology, NCI will request planning grant applications via an RFA. To be considered, an application must include the description of up to two pilot research projects in either nutrition and cancer therapy, nutrition and cancer biology, or nutrition and cancer cause and prevention. The grants would be funded for no more than 2 years at a maximum of $100,000 annually. Support beyond the 2-year period would require submission of traditional research grants (R01) and program project grants (P01).

In addition to these activities, a limited number of RFA's will be issued under the DNCP. Such activities will be undertaken cautiously, often after state-of-the-art meetings or following leads.

In cancer cause and prevention, a number of areas are to be investigated in an effort to understand the relationship of diet to cancer incidence: development of methods for identifying mutagens/carcinogens in food, body fluids, and feces; evaluation of cooking/processing methods relative to the formation of mutagens/carcinogens; determination of the role of classes of nutrients, vitamins, and minerals; and examination of dietary factors affecting exposure of carcinogens to target areas (e.g., gut mucosal lining). The intramural Environmental Epidemiology Branch is in the process of planning a number of studies relating diet to cancer incidence. Recommendations of the Workshop on Alcohol and Cancer are under review by the DNCP to determine the most satisfactory means of accomplishing the research recommendations.

Data analyses of past clinical studies on the role of nutritional supplementation related to cancer therapy are to be completed. The oat cell cancer study begun near the end of FY79 will be in full operation throughout 1981. This study will determine how nutritional support of patients with anaplastic small-cell carcinoma of the lung affects both the tumor and patient survival. Studies on the cachexia and anorexia of cancer patients will be continued.

Training in Nutrition

DNCP is considering the feasibility of developing a mechanism to stimulate investigation and institutional efforts in nutrition and oncology research. One such mechanism under consideration involves training researchers in nutrition and cancer. Another possible approach involves financial supplements to successful applicants among the 90 institutions which have NCI clinical education grants. The major thrust of the awards would be to develop nutrition education programs for medical and dental students at the undergraduate, graduate, and continuing education levels.

Based on approval/disapproval rates for grants in nutrition research, the critiques from grant summary statements, and opinions from study section members, the DNCP recognizes that the pool of investigators trained in both nutrition and oncology and the number of institutions committed to joint research are limited. Nutrition and oncology research requires interdisciplinary cooperation in areas where traditional links do not exist. In order to address this situation, the DNCP is considering the feasibility of developing special mechanisms to stimulate investigator and institutional efforts in such joint research. It is to be pointed out that these plans will remain tentative until they have received concept approval by divisional Advisory Groups. One mechanism under consideration involves training of researchers in nutrition and cancer. Through an RFA, NCI will request grant applications for institutional training and fellowships. The total commitment would be $500,000 for FY81 and FY82 for new grant starts.

Workshops

In FY81 the general approach to developing research strategies for specific areas of interest to the DNCP will be to hold conferences or workshops. This enables investigators to review the state of the art and work out research recommendations. Proceedings or a conference summary will be published in each case. Three conferences are scheduled: Significance of Diets in Animal Carcinogenesis Studies, Nutrition and the Pediatric Cancer Patient, and Nutrition and Breast Cancer.

Significance of Diet in Animal Carcinogenesis

A workshop planned for October 1980 will review the significance of diets in the carcinogenesis process. The results of this meeting will be published in the Journal of the National Cancer Institute.

Nutrition and the Pediatric Cancer Patient

Nutrition support of the child with cancer now is recognized as an important adjunct to cancer treatment. A workshop is scheduled for December 1980 to review the current state of the art and formulate future research needs and direction. Issues to be discussed include nutritional assessment, pathophysiology of anorexia and cachexia, tumoricidal potential of nutritional manipulation, and supportive nutritional intervention.

Proceedings of this workshop will appear in Cancer Research.

Nutrition and Breast Cancer

The DNCP, in conjunction with the Epidemiology Working Group of the Breast Cancer Task Force committee, is planning a working session on Diet and Breast Cancer Risk to be held in the spring of 1981. The objectives of this meeting will be to examine extant data in the question of diet as a risk factor for breast cancer and to discuss what kinds of future research might bring definitive answers to this question.

PROJECT DESCRIPTIONS

PROJECT DESCRIPTIONS

Identifying number: R01 CA 03728
Principal investigator: William S. Beck
Institution: Massachusetts General Hospital
Title: Metabolism of Normal and Leukemia Leukocytes

Total FY79 obligation: $115,973
Nutrition allotment: 100%
Nutrition funding: $115,973

Total FY80 obligation: $125,651
Nutrition allotment: 100%
Nutrition funding: $125,651

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

Current experiments are concerned with 1) biochemical mechanisms in the Killmann experiment - a critique of the "deoxyuridine suppression test"; 2) development of a sensitive enzymatic assay for picomole quantities to dTMP in tissue extracts; 3) studies on the incorporation of uracil into DNA; 4) studies of one-carbon metabolism of normal and leukemia leukocytes; 5) studies of folate and vitamin B_{12} uptake in cultured lymphocytes; 6) development of a new assay for folylpolyglutamate synthetase and partial purification of the enzyme from rat liver; 7) binding of human transcobalamins to rat liver cell fractions; and 8) studies of the microbiological (*Lactobacillus leichmannii*) assay for serum vitamin B_{12}: characterization of serum vitamin B_{12} analogs that are not detected by the microorganism.

Identifying number: R01 CA 07123
Principal investigator: Christine Waterhouse
Institution: University of Rochester
Title: Hepatic Synthesis and Release of Triglyceride

Total FY79 obligation: $51,620
Nutrition allotment: 100%
Nutrition funding: $51,620

Total FY80 obligation: $74,613
Nutrition allotment: 100%
Nutrition funding: $74,613

Cancer activity/thrust: Nutrition/Treatment Research

Hepatic Synthesis and Release of Triglyceride (continued)

Project description:

This project will study the interrelationship of carbohydrate and protein metabolism in subjects with metastatic cancer. Trace amounts of alanine, pyruvate, and glucose will be given to patients with metastatic malignant disease to obtain quantitative measurements of new glucose production, gluconeogenesis from amino acids, and Cori cycle activity. Concomitant study of glucose uptake and amino acid release from muscle will be done. Such studies will be carried out in the post absorption state, with glucose administration and after long-term parenteral administration of glucose and amino acids.

Identifying number: R01 CA 09599
Principal investigator: Lee W. Wattenberg
Institution: University of Minnesota, Minneapolis
Title: Microsomal Induction and Response to Carcinogens

Total FY79 obligation: $178,500
Nutrition allotment: 100%
Nutrition funding: $178,500

Total FY80 obligation: $127,200
Nutrition allotment: 100%
Nutrition funding: $127,200

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Certain naturally occurring compounds in foods are thought to inhibit chemical carcinogens. This study will investigate the mechanism of inhibition of naturally occurring indoles found in cruciferous plants such as cabbage and brussels sprouts. The investigation will also determine if plants other than cruciferae and which are part of the human diet have constituents that alter carcinogen metabolism. Among the other foods which will be evaluated are carrots and spinach.

Identifying number: R01 CA 10771
Principal investigator: Joseph Meites
Institution: Michigan State University
Title: Neuroendocrine Control of Mammary and Pituitary Tumors

Total FY79 obligation: $87,991
Nutrition allotment: 20%
Nutrition funding: $17,598

Total FY80 obligation: $92,034
Nutrition allotment: 20%
Nutrition funding: $18,407

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The overall objective is to determine the relation of the brain, particularly the hypothalamus, to development and growth of mammary and pituitary tumors and to utilize this information to inhibit such development and growth.

Since prolactin and estrogen are the principal hormones involved in development and growth of mammary tumors and, to a large extent, of pituitary tumors, and since these hormones are controlled directly (prolactin) or indirectly (estrogen) by the hypothalamus, the aim will be to experimentally alter hypothalamic function (by placing lesions or implanting hormones and drugs in the hypothalamus, by administration of drugs and hormones systemically, and by use of appropriate environmental stimuli) to inhibit or accelerate development and growth of these tumors in mice, rats, and dogs.

The effects of high- and low-fat diets, reduced caloric intake, and hypothalamic-induced obesity will be tested on serum hormone levels and the development and growth of mammary tumors.

The neuroendocrine mechanisms whereby pregnancy and lactation influence mammary tumor growth will be investigated. The effects of hypothalamic factors, hormones, and drugs on hormone secretion and growth of pituitary tumors will be studied. Old female rats also will be utilized, since they develop spontaneous mammary and pituitary tumors, which may be related to functional changes in hypothalamic functions in old rats.

The knowledge gained from these studies should prove useful in developing treatments for inhibiting the onset and/or growth of mammary and pituitary tumors in human subjects.

Identifying number: R01 CA 10917
Principal investigator: Charles Levinson
Institution: University of Texas Health Science Center, San Antonio
Title: Phosphate Transport and Metabolism in Carcinoma Cells

Total FY79 obligation: $39,611
Nutrition allotment: 100%
Nutrition funding: $39,611

Phosphate Transport and Metabolism in Carcinoma Cells (continued)

Total FY80 obligation: $43,312
Nutrition allotment: 100%
Nutrition funding: $43,312

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The theme of this project concerns the relationship between membrane transport of ions and the role of ions in the regulation of metabolic activity. The specific purpose of this study is to investigate the function of plasma membrane of the Ehrlich mouse ascites tumor cell in the control of inorganic phosphate transport and the relationship of this transport to the metabolism of phosphate. Since inorganic phosphate participates in energy metabolism and thereby differs from other inorganic anions, regulation of phosphate transport can be considered to be part of the general problem concerning the mechanism of permeation of other biologically important anions. Therefore, it is planned to investigate the role of membrane factors (surface charge density, electrical potential difference), as well as environmental factors in the regulation of anion transport. These efforts should provide a more complete understanding of the molecular events associated with the transport of phosphate and, indeed, other inorganic anions.

Knowledge of the regulation of phosphate transport and metabolism and its relation to metabolic control in tumor cells should provide greater insight into the central biologic problem of metabolic control.

Identifying number: R01 CA 11224
Principal investigator: Adalbert Koestner
Institution: Ohio State University
Title: Neurooncogenesis by Resorptive Carcinogens

Total FY79 obligation: $111,193
Nutrition allotment: 10%
Nutrition funding: $11,119

Total FY80 obligation: $102,926
Nutrition allotment: 10%
Nutrition funding: $10,293

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Neurooncogenic N-nitroso compounds will be used to develop an animal model of the induction of brain neoplasms. Studies relating to interactions of these compounds with cellular components and the immune system will be performed.

Identifying number: R01 CA 11339
Principal investigator: Charity Waymouth
Institution: Jackson Laboratory
Title: Control of Cell Growth, Differentiation, and Function

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: $61,918
Nutrition allotment: 100%
Nutrition funding: $61,918

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

Effort will be concentrated on cultivation in defined media of functional cells from mouse tissues, including liver, kidney, and prostate. The approaches will be by cell secretion, either in primary or later stages of culture, to reduce or eliminate nonepithelial cells. Methods for this will include differential cell attachment to a substrate, a property that is dependent both upon the type of cell and upon the composition, and treatment of the attachment surface: use of inhibitors of fibroblasts (e.g., hydrocortisone, cis-4-hydroxy-L-proline, Gentamicin) or of fibroblasts and lymphocytes (e.g., D-valine), or target-specific hormones that are promoters of particular types of epithelial cells. It is planned to continue refinement of the environment of the cell culture system, including adjustments in medium composition, with special attention to the substitution for sodium bicarbonate of nonbicarbonate buffers, either sodium glycerophosphate or, where that is not appropriate, other. With the use of media that are buffered other than with bicarbonate, the needs of cells for a source of CO_2, either provided as such or generated endogenously, e.g., from pyruvate, will be examined. Substitutes for L-glutamine will be tested to enable the media to be fully autoclavable. Other aspects of the environment to be examined are ion balance and osmolality (especially for kidney cells), where several cell types may be selected at different osomotic levels corresponding to the osmotic pressures to which they are exposed in vivo. Functions appropriate to the cell types studied will be tested, e.g., serum protein production by liver cells, and enzymes specific to each cell type.

Identifying number: R01 CA 12646
Principal investigator: Daniel Rudman
Institution: Emory University
Title: Abnormal Metabolism of Cancer Patients

Total FY80 obligation: $93,044
Nutrition allotment: 100%
Nutrition funding: $93,044

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

Tumor cells frequently synthesize and secrete proteins which are not normally present in body fluids. About 15 such tumor-related or tumor-specific proteins have so far been isolated. Each has provided a tool for diagnosis and management of a specific type of cancer. Recent advances in techniques of screening biologic fluids for proteins in specific molecular weight ranges indicate that urine and effusions of patients with advanced cancer contain a set of novel tumor-related proteins in molecular weight range 10,000 to 60,000. Purification and isolation of these proteins will develop a new series of antisera, each specific for a characterized cancer-related antigen. These antisera will provide new tests for early diagnosis of specific types of cancer; such tests will be inexpensive and suitable for mass screening of populations. Additional clinical applications of this project may be new information concerning 1) role of incomplete carbohydrate components of glycoproteins and glycolipids in determining metastatic properties of cancer cells, and 2) biochemical mechanisms responsible for progressive emaciation of patients with advanced cancer.

Identifying number: R01 CA 14146
Principal investigator: Lee W. Wattenberg
Institution: University of Minnesota
Title: Inhibition of Chemical Carcinogenesis

Total FY79 obligation: $66,818
Nutrition allotment: 100%
Nutrition funding: $66,818

Total FY80 obligation: $84,947
Nutrition allotment: 100%
Nutrition funding: $84,947

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The potential role of the antioxidants such as BHA in inhibiting chemical carcinogenesis will be studied in relation to DNA binding, carcinogen metabolism, and alteration of microsomal enzymes. The conditions under which this inhibition occurs will be determined, and the chemical characteristics which control the ability of antioxidants to exert an inhibitory influence will be derived.

Identifying number: R01 CA 14226
Principal investigator: William F. Benedict
Institution: Children's Hospital of Los Angeles
Title: Oncogenic and Mutagenic Potential of Antitumor Agents

Total FY79 obligation: N/A

Total FY80 obligation: $113,330
Nutrition allotment: 30%
Nutrition funding: $33,999

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

The early events of transformation are being studied in the C3H/10T1/2 cell line using cancer chemotherapeutic agents. In particular we are investigating transformation produced by 5-azacytidine as well as differentiation using the same 10T1/2 system. In addition, various inhibitors of transformation are being studied as well as their mechanism(s) of action. The production of sister chromatid exchanges by various cancer chemotherapeutic agents is also being investigated. Finally, we are studying the ability of various agents to block the induction of sister chromatid exchanges.

Identifying number: R01 CA 14260
Principal investigator: Lloyd B. Bullerman
Institution: University of Nebraska, Lincoln
Title: Molds and Mycotoxins in Foods

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Molds and Mycotoxins in Foods (continued)

Project description:

Studies of molds that produce ochratoxin and citrinin will continue and will include further verification of toxin production by molds isolated from cheese and cured meats, classification of these molds, and toxin production studies on foods and defined media. The effects of temperature on mold growth and mycotoxin production will be determined. Simultaneous mycotoxin production by individual molds and in mixed cultures will be studied. Stability of ochratoxin and citrinin in foods will be determined. Studies will continue on the effects of antifungal agents on toxic mold growth and on the mechanism of mold inhibition by sorbic acid.

Identifying number: R01 CA 14703
Principal investigator: Roland L. Phillips
Institution: Loma Linda University
Title: Epidemiology of Cancer in a Low-Risk Group

Total FY79 obligation: $602,443
Nutrition allotment: 100%
Nutrition funding: $602,443

Total FY80 obligation: $338,057
Nutrition allotment: 100%
Nutrition funding: $338,057

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

It is difficult to study the relation of diet to cancer in the United States due to the lack of uniformity in dietary practices. Seventh-Day Adventists (SDA's) are a conservative religious group that does not smoke or drink by church proscription, and about 50 percent of them do not use meat or coffee. SDA's are very health-oriented, and many of them use whole grains and other unrefined foods in abundance. For most cancer sites unrelated to smoking, previous studies have demonstrated that mortality rates in SDA's are about 70 percent of those for the general population.

This ongoing prospective study seeks to confirm these mortality differences with incidence data and to determine the specific component(s) of the SDA life style which account for the low risk of nonsmoking-related cancers in SDA's. Detailed information will be collected on demographic and lifestyle characteristics of 67,000 California SDA's over age 25. For 5 years, all deaths and new cancer cases will be monitored via annual contacts and review of hospital records for reported hospitalizations. Detailed characteristics and cancer incidence and survival rates of SDA's will be compared to those of a general population sample. Furthermore, a comparative analysis will be made of risk of major cancer types among subgroups of SDA's with different degrees of adherence, or duration of exposure, to various habits unique to SDA's (e.g., lifetime vegetarians vs. heavy meat consumers).

Identifying number: R01 CA 14881
Principal investigator: Ross Shiman
Institution: Pennsylvania State University
Title: Regulation of Tyrosine Synthesis in Hepatoma Cells

Total FY79 obligation: $76,876
Nutrition allotment: 100%
Nutrition funding: $76,876

Total FY80 obligation: $86,049
Nutrition allotment: 100%
Nutrition funding: $86,049

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The regulation of tyrosine synthesis in hepatoma cells growing in culture will be investigated. Both metabolic control (involving substrate and product levels, membrane transport properties) and genetic control (involving effects on protein synthesis and degradation) of the rate of hydroxylation of phenylalanine will be examined. The mechanisms of regulation of phenylalanine hydroxylase by cell population density and by hormones will be studied in detail. Primary rat hepatocytes and hepatoma cells will be examined for insight into the regulatory process and into differences between the normal and transformed cells.

Identifying number: R01 CA 15064
Principal investigator: Fun S. Chu
Institution: University of Wisconsin, Madison
Title: Immunochemical Studies on Carcinogenic Mycotoxins

Total FY79 obligation: $47,833
Nutrition allotment: 100%
Nutrition funding: $47,833

Total FY80 obligation: $46,469
Nutrition allotment: 100%
Nutrition funding: $46,469

Cancer activity/thrust: Immunology/Detection and Diagnosis

Immunochemical Studies on Carcinogenic Mycotoxins (continued)

Project description:

This project is to explore ways of maximizing the production of protective antibodies which will eliminate various carcinogenic mycotoxins from the body. Exposure to these toxins may occur through contaminated foods.

Identifying number: R01 CA 15305
Principal investigator: Richard G. Ham
Institution: University of Colorado
Title: Effect of Malignancy on Cell Growth Requirements

Total FY79 obligation: $88,008
Nutrition allotment: 100%
Nutrition funding: $88,008

Total FY80 obligation: $92,730
Nutrition allotment: 100%
Nutrition funding: $92,730

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

This research is organized around a search for differences between normal and malignant cells in their responses to nutrient and growth-regulating factors. The requirements for growth in culture of a variety of normal and malignant cells from humans, mice, rats, rabbits, and chickens will be studied, with major emphasis on cells of epithelial morphology. The requirement for serum proteins will be minimized by adjusting all components of the defined portion of the culture medium to experimentally determined optimum concentrations, by adding growth-promoting substances such as trace elements that are missing from many common media, by modifying the culture surface, by minimizing cellular damage during trypsinization, and by careful attention to all environmental factors. Elimination of nonspecific requirements for serum proteins will make it easier to isolate and characterize those factors that continue to be required by cells grown under the improved conditions. Each time the detailed requirements of a normal cell are worked out, they will be compared with those of chemically or virally transformed cells or spontaneous tumors of similar origin. The major objectives of the research are to define precisely the nutrient requirements of various normal cells, to develop improved media for use in research involving normal cells, and to identify differences between normal and malignant cells that might provide the basis for future clinical studies on the control of malignancy.

Identifying number: R01 CA 15541
Principal investigator: J. Lawrence Werther
Institution: Mount Sinai School of Medicine
Title: Absorption of Carcinogens and Mucosal Barrier Function

Total FY79 obligation: $60,667
Nutrition allotment: 100%
Nutrition funding: $60,667

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

With the recently available advances in chemical carcinogenesis in laboratory animals and availability of techniques to measure gastric mucosal permeability and gastric function, a model of a dietary carcinogen will be studied with respect to those conditions which seemingly predispose humans to gastric carcinoma.

The aim is to 1) measure the absorption of this agent from canine gastric pouches under "normal" conditions for such a model; 2) measure changes in the rate of absorption of the carcinogen during the course of months so that the gastritis which it produces can itself be evaluated in relation to barrier function and increased carcinogen absorption; 3) measure absorption of the carcinogen when the barrier is acutely disrupted by bile or aspirin acid solutions; 4) produce chronic inflammatory change and persistent barrier dysfunction in canine pouches by means of repeated bile acid instillations and, after this is accomplished and verified, to measure absorption of the carcinogen; 5) quantitate changes in mucosal barrier function resulting from the gastritis and intestinal metaplasia produced by the carcinogen and to relate these anatomical changes to the physiochemical ones; and 6) measure absorption rates (and test effectiveness) of carcinogens that are not ordinarily well absorbed by the stomach and yielding only poor rates of cancer production in the glandular stomach in laboratory animals.

The hypothesis that certain dietary carcinogens may not ordinarily be absorbed into the gastric mucosa and are not effective there because of the normal function of mucosal barrier will be tested.

Identifying number: R01 CA 15664
Principal investigator: Stanley Goldfarb
Institution: University of Wisconsin, Madison
Title: Cholesterol Metabolism in Hepatic Neoplasms

Total FY79 obligation: $65,792
Nutrition allotment: 10%
Nutrition funding: $6,579

Cholesterol Metabolism in Hepatic Neoplasms (continued)

Total FY80 obligation: $8,348
Nutrition allotment: 10%
Nutrition funding: $835

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Mouse and rat putative premalignant hepatocellular lesions are to be studied by a variety of histochemical techniques in order to learn whether or not oncogenesis proceeds in a sequential fashion. Enzymatic markers to be studied include ATPase, gamma-glutamyltranspeptidase, glucose-6-phosphatase, and alkaline phosphatase. Histochemical data will be combined with [^{3}H]thymidine-labeling indices in order to characterize phenotypically different populations of cells. In addition, the in vivo and in vitro regulation of cholesterol and bile acid synthesis as reflected by activities of HMG CoA reductase and cholesterol 7-alpha-hydroxylase will be studied in fully developed hepatomas and preneoplastic lesions.

Identifying number: R01 CA 15813
Principal investigator: Nome Baker
Institution: University of California School of Medicine, Los Angeles
Title: Lipid Transport Synthesis and Metabolism in Cancer

Total FY79 obligation: $71,497
Nutrition allotment: 100%
Nutrition funding: $71,497

Total FY80 obligation: $75,715
Nutrition allotment: 100%
Nutrition funding: $75,715

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The overall objective of this project is to study the fatty acid transport from adipose tissue and other host tissue lipids directly to cancer cells by pathways which do not involve plasma-free fatty acids (FFA) as intermediates. The metabolic controls which may effect such direct transport will also be examined.

A major aim of this study will be to define the pathways involved in the conversion of dietary fat to cancer cell lipid and to quantify the relative importance of dietary lipids to the metabolic economy of the cancer cell. Further investigation of lipogenic activation by dietary carbohydrate in cancers of mice fed fat-free, high-carbohydrate diets will be undertaken.

Identifying number: R01 CA 15860
Principal investigator: Joseph Roberts
Institution: Sloan-Kettering Institute for Cancer Research
Title: A Program for Development of New Antitumor Enzymes

Total FY79 obligation: $75,539
Nutrition allotment: 20%
Nutrition funding: $15,108

Total FY80 obligation: $19,795
Nutrition allotment: 20%
Nutrition funding: $3,959

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

Overall Objectives: 1) Continue to study the biochemical, physical and biological properties of antitumor glutaminases, with emphasis on those characteristics which may be important for good therapeutic activity. 2) Bacterial enzymes have been isolated in our laboratory which degrade plasma histidine, serine and arginine when injected in mice. We will purify these enzymes and study their effects on growth of experimental tumors. 3) Test known organisms and those isolated from soil by the enrichment culture technique for production of the following enzymes: a) a cystine-degrading enzyme capable of depleting plasma cystine in vivo; b) enzymes which will attack the polyamines (putrescine, spermidine and spermine) in vivo--we wish to test the antineoplastic effects of polyamine-degrading enzymes alone and in combination with chemical analogues, which inhibit polyamine biosynthesis; c) a neuraminidase with optimal activity at physiological pH and other characteristics which are needed for maximum therapeutic usefulness. 4) Study the effects of prolonged enzyme treatment on plasma and tissue concentrations of their substrates in animals. 5) Evaluate the antineoplastic efficacy of single- and multi-enzyme therapy, as well as enzyme therapy combined with appropriate chemical analogs. 6) Determine the toxicity of new enzymes in animals. 7) If needed, chemically or physically modify the enzymes to extend their biological half-life, reduce their immunogenicity and improve their distribution outside the vascular space so as to increase their effectiveness on solid tumors.

Identifying number: R01 CA 16060
Principal investigator: Walter Troll
Institution: New York University
Title: Inhibition of Tumor Promotion by Protease Inhibitors

Total FY79 obligation: $118,368
Nutrition allotment: 100%
Nutrition funding: $118,368

Total FY80 obligation: $121,747
Nutrition allotment: 100%
Nutrition funding: $121,747

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Protease inhibitors are known to modify development of tumors at both stages of two-stage carcinogenesis of mouse skins. Consumption of soybeans which contain these inhibitors may be responsible for the low incidence of breast cancer in Japanese and Seventh-Day Adventist populations. This hypothesis will be tested by feeding soybean trypsin inhibitor to mice in two-stage carcinogenesis experiments and to rats exposed to ionizing radiation.

Identifying number: R01 CA 16442
Principal investigator: Morris H. Ross
Institution: Institute for Cancer Research, Philadelphia
Title: Regulation of Tumor Susceptibility

Total FY79 obligation: $115,181
Nutrition allotment: 100%
Nutrition funding: $115,181

Total FY80 obligation: $165,923
Nutrition allotment: 100%
Nutrition funding: $165,923

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

These studies are designed to establish whether or not knowledge of each individual's "optimal" tumor-promoting diet can be used to decrease the risk of spontaneous neoplasia by dietary manipulations and to what extent genetic factors determine the optimal tumor-promoting diet of each individual. The role of self-selection of the diet in maximizing tumor risk will be studied.

Identifying number: R01 CA 16631
Principal investigator: Harriett K. Meiss
Institution: New York University
Title: Isolation and Analysis of DNA Mutants of BHK Cells

Total FY79 obligation: $87,298
Nutrition allotment: 5%
Nutrition funding: $4,365

Total FY80 obligation: $110,879
Nutrition allotment: 5%
Nutrition funding: $5,544

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

Mammalian DNA replication in the hamster fibroblast cell line BHK21 is being studied. Amino acids are manipulated in vitro to control different stages of the cell cycle thus allowing the study of specific genetic control of replication.

Identifying number: R01 CA 16650
Principal investigator: Ray B. Durwood
Institution: Case Western Reserve University
Title: Hormonal Control of Normal and Neoplastic Breast Cells

Total FY79 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

This work involves the utilization of long-term and short-term monolayer cultures of normal and neoplastic mammary cells to determine precisely the action of hormones on differentiation and secretory function of normal breast tissue and the manner in which they may regulate the growth of mammary neoplasms. The synthesis and secretion of milk components (proteins, carbohydrates, and lipids) will be assessed by various biochemical techniques. Morphological criteria will be established by electron and light microscopy in the classification of hormone-responsive normal and neoplastic cells.

Hormonal Control of Normal and Neoplastic Breast Cells (continued)

Studies will be done to evaluate the steps at which hormonal alterations in cell metabolism are regulated and to biochemically define these regulatory mechanisms. Studies to evaluate the involvement of cyclic AMP metabolism will be included.

Identifying number: R01 CA 16788
Principal investigator: Chung S. Yang
Institution: College of Medicine and Dentistry of New Jersey
Title: Monoxygenase: Properties and Carcinogen Activation

Total FY79 obligation: $60,629
Nutrition allotment: 15%
Nutrition funding: $9,094

Total FY80 obligation: $85,343
Nutrition allotment: 15%
Nutrition funding: $12,801

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The cytochrome P-450-containing monoxygenase enzyme system is known to play a key role in the activation of carcinogens.

This project is a continuation of current studies designed to characterize the properties of the nucelar monoxygenase system and assess its role in the metabolism of benzo[a]pyrene (a carcinogenic hydrocarbon) and aflatoxin B_1 (a natural food toxicant). The binding of the metabolism activated benzo[a]pyrene and aflatoxin B_1 to nuclear DNA, RNA, histones, and nonhistone proteins will be studied with the use of isolated rat liver nuclei. The effect of microsomes on the binding will be studied systematically to assess the roles of microsomes and nuclei in foodborne carcinogen activation.

Identifying number: R01 CA 16827
Principal investigator: Edward J. Herbst
Institution: University of New Hampshire
Title: Polyamines as Metabolic Indicators of Carcinogenesis

Total FY79 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Nitrosamines capable of inducing liver and kidney tumors in rats and mice will be administered in single or multiple doses. Relationships between the incidence of tumors and ornithine decarboxylase activity will be investigated by modifying the enzyme activity during the course of tumor development. Enzyme activity will be altered by dietary means, by the feeding of toxicants, and by the administration of enzyme inhibitors. The effect of nitrosamines on the synthesis of macromolecules by target tissues and the time course of changes in their synthesis during nitrosamine carcinogenesis will be studied. Modifications in polyamine biosynthetic enzymes and polyamines during the development of tumors in target tissues will be determined. The relationship between the induction and promotion of tumors and polyamine metabolism in target tissues of nitrosamines will be ascertained.

Identifying number: R01 CA 16904
Principal investigator: Kato L. Perlman
Institution: University of Wisconsin
Title: Microbial Metabolite Inhibition of Tumor B_{12} Binding

Total FY79 obligation: $54,182
Nutrition allotment: 15%
Nutrition funding: $8,127

Total FY80 obligation: Active, not funded
Nutrition allotment: 15%
Nutrition funding: None

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

The objective of the research is to determine whether the observation that certain fermentation cultures elaborate low molecular weight, amino acid-containing substances which interfere with the binding of vitamin B_{12} by bacterial and mammalian cells offers promise of a new type of chemotherapeutic agent effective against tumor cells.

Identifying number: R01 CA 17037
Principal investigator: Barry E. Ledford
Institution: Medical University of South Carolina
Title: Serum Protein Synthesis by Mouse Hepatoma Cells

Total FY79 obligation: $43,701
Nutrition allotment: 5%
Nutrition funding: $2,185

Total FY80 obligation: $3,832
Nutrition allotment: 5%
Nutrition funding: $192

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The overall objective of this research is to study the regulation of serum protein synthesis in cultured mouse hepatoma cells (Hepa). The experimental situations to be investigated are designed to simulate physiological changes believed to regulate serum protein synthesis in the liver. Additionally, studies of the effects of specific antibodies on antigen synthesis will be conducted. The objective of these latter experiments is to understand the role of antibodies in the development of hepatocarcinoma.

The cell line (Hepa) to be used in these investigations was derived from the mouse hepatoma BW7756 (Jackson Laboratory). These cells secrete albumin, alpha-fetoprotein, and transferrin into the culture medium. The rates at which the proteins are synthesized and secreted depend upon growth conditions.

The following regulatory phenomena will be studied in Hepa: 1) autoregulation of albumin synthesis, 2) effects of essential amino acids on albumin synthesis, 3) effects of cyclic AMP on serum protein synthesis, and 4) the effects of antibodies to specific proteins on the synthesis of their antigens. The experimental parameters to be evaluated are 1) cellular rate of synthesis (molecules/cell/minute), 2) polyribosome size, and 3) translation rate (polypeptides/minute). These measurements will allow the calculation of two additional parameters: 1) the rate of ribosome initiation on specific mRNA's and 2) the number of functional mRNA molecules per cell.

Identifying number: R01 CA 17283
Principal investigator: Charles P. Burns
Institution: University of Iowa
Title: Lipid Metabolism of Leukocytes

Total FY79 obligation: $60,432
Nutrition allotment: 100%
Nutrition funding: $60,432

Total FY80 obligation: $64,602
Nutrition allotment: 100%
Nutrition funding: $64,602

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

Changes in the fat composition of the diet fed to tumor-bearing mice alter the lipid composition of L1210 murine leukemia cells growing in these mice. This project is designed to examine the effect of diet-induced alterations of the lipid composition of membranes on cell function. The phospholipids of the cell membranes would be of special interest, since changes in them might result in variations in membrane properties and functions, including the transport of antineoplastic drugs. The hypothesis will be examined in two systems: 1) L1210 mouse leukemia cells from animals fed either a high saturated or polyunsaturated fat diet, and 2) leukocytes obtained from normal human volunteers fed either a high saturated or polyunsaturated fat diet. In the animal model, the median survival of animals carrying the L1210 leukemia cells and receiving concurrent antineoplastic drugs will be compared for those animals receiving either a high saturated or polyunsaturated fat diet. Changes in membrane lipids which occur in the neoplastic cells from these animals will be characterized, and these changes will be analyzed in relation to changes in membrane physical properties such as fluidity. In addition, the function of enzymes located within or upon the membrane and the transport of drugs across the membrane will be examined. The function of leukocytes from normal human subjects on experimental diets will be examined (phagocytosis, chemotaxis, incorporation of fatty acid, transport of drugs as well as the membrane lipid changes that result from the diets).

Identifying number: R01 CA 17332
Principal investigator: Richard M. Halpern
Institution: University of California, Los Angeles
Title: Accessible Metabolic Pathways of Neoplastic Cells

Total FY79 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Diagnostic Research/Detection and Diagnosis

Accessible Metabolic Pathways of Neoplastic Cells (continued)

Project description:

The discovery that methylation of homocysteine is impaired in malignant and embryonic cells but not in normal cells in tissue culture has directed our attention to the metabolism of folic acid and its derivatives. A cleavage system has been detected that accounts for the formation of pterin-6-carboxaldehyde as a degradation product of folic acid found only in malignant cells. In addition to the production of pterin-6-carboxaldehyde in tissue culture, a high correlation has been demonstrated between its excretion in the urine and the occurrence of malignant disease in individuals.

Methods will be examined of quantitatively determining pterin-6-carboxaldehyde by high-pressue liquid chromatography and purifying from malignant tissue the enzyme system responsible for its production.

Identifying number: R01 CA 17389
Principal investigator: Hubert J. Wolfe
Institution: Tufts University
Title: C-Cell Hyperplasia and Medullary Carcinoma of Thyroid

Total FY79 obligation: N/A

Total FY80 obligation: $124,946
Nutrition allotment: 5%
Nutrition funding: $6,247

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The syndrome of familial medullary thyroid carcinoma is inherited as an autosomal dominant trait and is characterzed by the development of bilateral and multicentric C-cell and adrenal medullary tumors. Sequential clinical screening studies for determination of calcitonin and catecholamine levels in these kindreds, combined with correlative pathological analyses, have led to the concept that both these tumors are preceded by relatively long preneoplastic phases of C-cell and adrenal medullary hyperplasia. The human tumor system, together with similar experimental animal models, provides an opportunity to study the early phases of neoplastic growth and to delineate the differences between physiological and preneoplastic (pathological) hyperplasia in vivo and in vitro. Alterations in cell junctions (desmosomes), abnormalities in the basal lamina, and heterogeneity in secretory granule morphology will be correlated with tissue and serum calcitonin heterogeneity and other peptide hormone production by radioimmunoassay, immunocytochemistry and morphometric analyses, with the progressive phases of preneoplastic and neoplastic development. In vitro studies of the effects of various agents on modulation of peptide hormone synthesis and secretion will be undertaken in normal, hyperplastic and neoplastic cells.

Identifying number: R01 CA 17747
Principal investigator: Phillip B. Hylemon
Institution: Virginia Commonwealth University
Title: Bile Salt Catabolism Regulation by Intestinal Bacteria

Total FY79 obligation: $40,980
Nutrition allotment: 100%
Nutrition funding: $40,980

Total FY80 obligation: $43,470
Nutrition allotment: 100%
Nutrition funding: $43,470

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Dietary environmental factors are considered to be involved in the etiology of colon cancer. The overall objective of this grant is to delineate the role of bile acids and intestinal microflora in colon cancer carcinogenesis.

Identifying number: R01 CA 18151
Principal investigator: Jack G. Stevens
Institution: University of California, Los Angeles
Title: Analysis of the Shope Papilloma-Carcinoma System

Total FY79 obligation: $100,249
Nutrition allotment: 5%
Nutrition funding: $5,012

Total FY80 obligation: $103,317
Nutrition allotment: 5%
Nutrition funding: $5,166

Cancer activity/thrust: Viral Oncology/Cause and Prevention

Analysis of the Shope Papilloma-Carcinoma System (continued)

Project description:

The Shope papilloma-carcinoma system has great potential in definition of basic biochemical phenomena that are critical to the neoplastic process in domestic and cottontail rabbits in which a viral-induced progression from normal skin yields papilloma which yields carcinoma. It has been shown that multiple copies of the viral genome are conserved in all neoplasms and that about 5 percent of viral genetic information is transcribed in tumors of domestic rabbits (which characteristically do not produce virus). It has also been shown that multiple copies of the virus genome are present in viral superinfected chemically induced papillomas and in serially transplantable VX-2 and VX-7 carcinomas.

In the present application it is planned to determine 1) whether the same transcripts are present in all tumors; 2) whether or not the viral DNA is covalently integrated into the host cell genome; 3) if there is a translation product in these tumors and, if so, its basic properties (since it is likely to be involved in an induction and maintenance of the neoplastic state); 4) the viral-specific macromolecular events which accompany malignant change induced by the virus in superinfected papillomas established by a chemical carcinogen and, in related studies, the effect of a tumor promoter on the expression of viral genes will be assessed; 5) if VX-2 and VX-7 carcinomas resemble the primary tumors with respect to viral gene expression (should this prove to be the case, cultures of these cells will be intensively studied to determine the nature of the virus cellular relationship as it relates to these neoplastic cells); 6) if, with the use of additional methods, cell lines from the virus tumors can be established in vitro. Molecular hybridization, restriction endonuclease digestion, immunoprecipitation of radioactive materials, and cell culture methods appropriate to epidermal cells will be the primary tools employed in these studies.

Identifying number: R01 CA 18205
Principal investigator: Robert C. Johnson
Institution: Medical University of South Carolina
Title: Radiosensitization by Specific DNA Repair Control

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Cancer activity/thrust: Cancer Biology/Radiation

Project description:

This study will attempt to determine the degree to which low dose radiation is potentiated by attraction of recA/exr mediated repair by drugs, nutrition, and physical methods.

Identifying number: R01 CA 18263
Principal investigator: Brahma P. Sani
Institution: Southern Research Institute
Title: Retinoic Acid-Binding Protein

Total FY79 obligation: $16,450
Nutrition allotment: 100%
Nutrition funding: $16,450

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The genetic role of retinoic binding protein and the protein-ligand complex will be elucidated in more detail. Quantities of retinoic acid-binding protein will be purified with the use of standardized procedures in order to immunize rabbits for the production of specific antiserum. The effect of the binding protein on the binding of retinoic acid to chromatin and to DNA isolated from retinoid-responsive and nonresponsive tissues will be studied. The binding constant of retinoic acid to RABP and the effect of pH, ions, and temperature on the ligand-protein interactions will be determined.

Identifying number: R01 CA 18575
Principal investigator: Thomas P. Stein
Institution: University of Pennsylvania
Title: Surgery and Adjuvant Cancer Therapy

Total FY79 obligation: $89,489
Nutrition allotment: 100%
Nutrition funding: $89,489

Surgery and Adjuvant Cancer Therapy (continued)

Total FY80 obligation: $90,906
Nutrition allotment: 100%
Nutrition funding: $90,906

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

Some cancer patients die from the effect of the cancer-associated cachexia rather than the tumor per se. Because cachexia and progressive weight loss can occur in patients with quite small tumors, it is currently believed that these effects are the results of a systemic effect of the tumor on the host.

The objective of this project is to test the hypothesis that a tumor-induced amino acid imbalance is responsible for some of the effects of a tumor on the host. A totally parenterally nourished tumor-bearing rat model will be given one of five parenteral diets containing different amino acid mixtures. The three main assays to be used are 1) nitrogen retention, 2) glucose turnover, and 3) muscle protein fractional synthesis rates.

Identifying number: R01 CA 18618
Principal investigator: George W. Harrington
Institution: Temple University
Title: Electroanalytical Studies of N-Nitrosamines

Total FY79 obligation: $62,772
Nutrition allotment: 100%
Nutrition funding: $62,772

Total FY80 obligation: $64,054
Nutrition allotment: 100%
Nutrition funding: $64,054

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Differential pulse polarography [illegible] be utilized to determine N-nitrosamines of varying structures singly and in mixtures. These determinations will be performed in pure aqueous solutions and in biological fluids. This technique will be applied to the study of nitrosamine carcinogenesis inhibitors such as ascorbic acid.

Identifying number: R01 CA 18664
Principal investigator: Yagya N. Sinha
Institution: Scripps Clinic and Research Foundation
Title: Role of Prolactin in Mouse Mammary Tumorigenesis

Total FY79 obligation: $72,560
Nutrition allotment: 25%
Nutrition funding: $18,140

Total FY80 obligation: $87,168
Nutrition allotment: 25%
Nutrition funding: $21,792

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

This study has four major goals. 1) The role of prolactin and growth hormone will be investigated in relation to genetic, viral, chemical, and nutritional factors in the development of mammary tumors in mice. 2) The dynamics of prolactin secretion (induced with perphenazine or breast nursing) and metabolic clearance rates (MCR) will be compared after foster nursing (MTV introduction) between mice of high- and low-incidence strains, after administration of chemical carcinogens, and after the induction of obesity. Prolactin and growth hormone will be measured by specific and homologous radioimmunoassay for the two hormones. 3) The modulation of prolactin and growth hormone receptor activities in the mammary gland by genetic, viral, hormonal, and nutritional variables will be investigated. Mammary receptor activities will be measured by in vitro incubation of mammary plasma membrane fractions with mouse prolactin and growth hormone iodinated with lactoperoxidase. 4) The influence on mammary tumor growth of immunization against mouse prolactin and growth hormone by administering purified antimouse prolactin and antigrowth hormone gamma-globulins will be studied.

Identifying number: R01 CA 18691
Principal investigator: John P. Lambooy
Institution: University of Maryland, Baltimore
Title: Covalent Bonding of Flavins in Neoplastic Tissue

Total FY79 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Covalent Bonding of Flavins in Neoplastic Tissue (continued)

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

Among the analogs of riboflavin that have been synthesized, two are utilized by rats for their flavoprotein enzymes when no other flavin is available. The activities of the two homologs for several enzymes are very like that of riboflavin; however, in the case of succinic acid dehydrogenase (SDH), the activities of the two homologs and the vitamin are remarkably different. One of the homologs causes a substantial retardation (50 percent) in the growth rate of Walker rat carcinoma 256. This reduction correlates with the loss of activity of SDH in these tumors. These differences may be best explained by possible differences in the abilities of the three flavins to become covalently bound to the enzyme.

The purpose of this project is to synthesize these two homologs labeled with ^{14}C and administer them to experimental animals. The radioactivity of the flavin covalently bound to the enzyme in the mitochondria of the tumor can be determined after the removal of all flavin not covalently bound. The radioactivity would be correlated with the enzyme activity. To compare with data accumulated on the influence of these two flavins on the enzymes of the liver, the same evaluation would be made of the bound flavin in the mitochondria of the liver.

Besides SDH, the mammalian mitochondron contains monoamine oxidase (MAO). This MAO also binds flavin covalently. For this reason it will be necessary to make use of known procedures for separating these two enzymes, at least in the case of the liver. Although unknown at present, it is assumed that the same would be true for the tumor tissue. Correlation of the enzyme activity and the radioactivity would be determined for the MAO also.

Identifying number: R01 CA 18817
Principal investigator: A. Subbayya Shetty
Institution: Florida Agriculture and Mechanical University
Title: Enzymatic Detoxification of Hydroxyanthranilic Acid

Total FY79 obligation: $35,709
Nutrition allotment: 25%
Nutrition funding: $8,927

Total FY80 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The enzymatic breakdown of hydroxyanthranilate by hydroxyanthranilate oxygenase will be studied in control and pyridoxine-deficient mice. The mutagenicity of tryptophan metabolites will be studied.

Identifying number: R01 CA 18844
Principal investigator: Joseph Roberts
Institution: Sloan-Kettering Institute for Cancer Research
Title: Therapy by Enzymatic Depletion of Essential Amino Acids

Total FY79 obligation: $72,618
Nutrition allotment: 100%
Nutrition funding: $72,618

Total FY80 obligation: $86,366
Nutrition allotment: 100%
Nutrition funding: $86,366

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

This study is designed to develop appropriate techniques for the production, isolation, and purification of enzymes that possess certain predetermined characteristics and are capable of degrading specific essential animo acids, that is, tryptophan, lysine, threonine, and phenylalanine in vivo. The antineoplastic efficacy of enzyme therapy as well as the effects of prolonged enzyme treatment on plasma and tissue stores of amino acids in animals will be evaluated.

Identifying number: R01 CA 19015
Principal investigator: Harold Amos
Institution: Harvard University
Title: Sugars, Glycoproteins: Normal and Malignant Cells

Total FY79 obligation: $113,502
Nutrition allotment: 100%
Nutrition funding: $113,502

Total FY80 obligation: $155,745
Nutrition allotment: 100%
Nutrition funding: $155,745

Cancer activity/thrust: Nutrition/Cancer Biology

Sugars, Glycoproteins: Normal and Malignant Cells (continued)

Project description:

The overall objective of the experiments is to alter in specific ways the mammalian cell phenotype by manipulating the hexose environment. The assumption is made that the oligosaccharide composition of cells, hence the composition of their glycolipids and glycoproteins, is dependent to some extent upon the specific pool of nucleotide sugars in the cells. Good evidence is available to indicate that the pool of nuceotide sugars can in fact be modified both by the sugars fed to cells, and by nucleoside analogs. In addition, it can be demonstrated that growth on specific sugars in lieu of glucose results in marked changes in 1) hexose transport; 2) concanavalin A binding capacity; 3) average length of oligosaccharides in surface glycoproteins; 4) morphology and surface architecture of cells as revealed by scanning electron microscopy. The use of sugar analogs or nuceloside analogs, or both, might result in differential glycosylation or oligosaccharide synthesis by cells. It is planned to exploit the potential variation in glycosyl-transferase enzyme properties (including specificity for substrate and carrier) to reduce selectively the malignancy or increase the immunogenicity of tumor cells in situ.

Identifying number: R01 CA 19126
Principal investigator: Herbert Lazarus
Institution: Sidney Farber Cancer Institute
Title: Implications of Cystine Auxotrophy in Human Malignancy

Total FY79 obligation: $110,567
Nutrition allotment: 100%
Nutrition funding: $110,567

Total FY80 obligation: $114,488
Nutrition allotment: 100%
Nutrition funding: $114,488

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

Evidence has been collected which indicates that at least some cultured human leukemia cells and cultured as well as freshly isolated rodent leukemia cells have an absolute nutritional requirement for preformed L-cystine. In essence, they behave phenotypically like cystine auxotrophs. The biochemical basis for this growth requirement appears to be, at least in part, an intracellular depletion of cystathionase (CSE), the enzyme that catalyzes the last step in the L-CYS biosynthetic pathway.

The goal is to determine the prevalence of the CYS /CSE phenotype among freshly isolated human tumor cells from patients with both hematologic malignancy and solid tumor diseases, and also to determine whether, in certain instances, this phenotype is specific to tumor, as opposed to normal cells.

With the use of a specific cystathionase radioimmunoassay, the question of whether CYS /CSE cells synthesize less CSE protein than CYS /CSE cells will be addressed. If so, a fluorescence-activated cell sorter and fluorescent-labeled anti-CSE IgG will be used to develop a sorting method that can discriminate between CSE and CSE cells. The goal of such an effort would be the ability to detect otherwise occult tumor cells in readily accessible cell reservoirs in the body. Cystine-degrading enzymes may provide a therapeutic approach to certain human tumors.

Identifying number: R01 CA 19305
Principal investigator: Hans-Jorg Heiniger
Institution: Jackson Laboratory
Title: Cholesterol in Normal and Malignant Lymphocytes

Total FY79 obligation: N/A

Total FY80 obligation: $95,016
Nutrition allotment: 100%
Nutrition funding: $95,016

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Membrane-bound cholesterol in lymphocytes can be manipulated by treating these cells with oxygenated derivatives of cholesterol, which specifically depress the de novo synthesis of cholesterol. Inhibition of cholesterol synthesis in lymphocytes abolishes their DNA synthesis and thus interferes with cell division. This study will especially focus on the effects of such treatments on the cell-mediated and humoral immune response in the intact animal as well as on their effects upon the growth of transplanted and spontaneous tumors.

Identifying number: R01 CA 19389
Principal investigator: Margaret C. Neville
Institution: University of Colorado Medical Center
Title: Nutrient Uptake in Normal and Tumorous Mammary Gland

Total FY79 obligation: $42,207
Nutrition allotment: 100%
Nutrition funding: $42,207

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This is an investigation into the specificity of amino acid transport in mouse mammary gland. A quantitative test for the specificity of the A-sites and L-sites will be developed and applied to glands from pregnant and lactating mice as well as to mouse mammary tumors in vitro.

Identifying number: R01 CA 19496
Principal investigator: Thomas M. Mack
Institution: University of Southern California
Title: Case-Control Study of Carcinoma of the Esophagus

Total FY79 obligation: $81,281
Nutrition allotment: 100%
Nutrition funding: $81,281

Total FY80 obligation: $99,463
Nutrition allotment: 100%
Nutrition funding: $99,463

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This is a grant to study the epidemiology of carcinoma of the esophagus, to test previously suggested causal hypotheses and associations, to discover new associations, and to delineate the characteristics of the high-risk groups. This is a large case-control study being performed prospectively in Los Angeles County. It has been designed to permit simultaneous examinations of multiple antecedent risk factors. Patients with cancer of the esophagus are identified by the LAC/USC Cancer Surveillance Program. A questionnaire is used to obtain data on environmental exposures, tobacco and alcohol consumption, diet, occupation, and medical history and treatment. It is administered to both patients and neighborhood controls as soon as possible after the cases have been diagnosed. Standard matched-pair analyses of multiple variables will be performed on the data from the questionnaire.

Identifying number: R01 CA 19519
Principal investigator: Jacques R. Chipault
Institution: University of Minnesota, St. Paul
Title: Diet, Fecal Steroids, and Colon Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The effect of diet on fecal and intestinal glucuronidase and hydroxylases will be studied in reference to their possible relationship to the incidence of colon cancer.

Identifying number: R01 CA 19523
Principal investigator: Richard T. Hamilton
Institution: Salk Institute for Biological Studies
Title: Comparison of Transport in Normal and Transformed Cells

Total FY79 obligation: $100,773
Nutrition allotment: 100%
Nutrition funding: $100,773

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

With the objective of determining the extent of participation of nutrient transport in cellular growth control, membrane vesicles from fibroblasts (3T3, SV3T3, CEF) have been isolated in culture. These

Comparison of Transport in Normal and Transformed Cells (continued)

membranes transport phosphate by a saturable process. They also demonstrate sodium-gradient stimulated alpha-amino isobutyric acid uptake.

With membrane vesicles isolated from normal and transformed cells the molecular mechanisms of transport will be compared to determine those changes which occur upon neoplastic transformation. Membranes isolated from temperature-sensitive transformed cells at various stages of transformation will be studied.

These studies will include a correlation of the effect of serum and purified growth factors on the isolated transport system with the growth stimulatory effect of serum on whole cells. The mechanisms by which these growth stimulators effect the transport of nutrients by the cell surface will be investigated.

Identifying number: R01 CA 19988
Principal investigator: Isadore A. Bernstein
Institution: University of Michigan
Title: In Vitro Chemical Carcinogenesis

Total FY79 obligation: Active, not funded
Nutrition allotment: 5%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 5%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This project will utilize existing mouse and rat epidermal systems for developing a suitable protocol(s) for human subjects. The approach to this problem will be to induce malignant transformation in animal in vitro systems; to identify nutritional, morphologic, ultrastructural, biochemical, and enzymatic markers coincident with malignant transformation; to identify early markers that precede malignant transformation but need not be causal to it; and to correlate the appearance of early markers with malignant transformation in vivo and in vitro with strains of mice and rats that vary in susceptibility to known carcinogens. Early markers that correlate with malignant transformation in epidermal systems will also be tested for coincidence in other organs.

The long-term objective of this research project is to identify early markers of malignant transformation for an epidemiological survey of human populations.

Identifying number: R01 CA 20040
Principal investigator: Delano V. Young
Institution: Boston University
Title: Transformed Cell Growth: Serum Peptide and Lipid Factors

Total FY79 obligation: $10,839
Nutrition allotment: 25%
Nutrition funding: $2,710

Total FY80 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The overall objective of this project is to understand the growth factor requirements of SV3T3 cells in culture. Specifically, the work focuses on the purification and chemical and biological characterization of a low molecular weight (500-1,000) serum growth factor designated peak III. Peak III has been partially purified by a method suitable for the treatment of bulk quantities of serum and by conventional gel filtration. New purification steps are being sought. The chemical nature of peak III is presently obscure (no hexoses or amino acids). Further chemical analysis will include NMR and IR spectroscopy, gas chromatography coupled with mass spectrometry, elemental analysis, and other suitable microtechniques. Since peak III does not affect the rates of DNA or RNA synthesis, it appears that it is more accurately described as a viability agent rather than as a growth factor. Other tests of its biological ability will include its effect on carbohydrate metabolism and nutrient uptake.

The identification of another major serum growth factor ("peak I") will be approached by comparison with a number of newly discovered growth-active proteins. Finally, attempts will be made to replace serum completely through the use of media supplemented with these SV3T3 growth and viability factors.

Identifying number: R01 CA 20079
Principal investigator: Colin T. Campbell
Institution: Cornell University
Title: Effect of Nutrition on Carcinogen and Toxin Metabolism

Total FY79 obligation: $94,338
Nutrition allotment: 100%
Nutrition funding: $94,338

Total FY80 obligation: $5,353
Nutrition allotment: 100%
Nutrition funding: $5,353

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The role of nutrition on the metabolism of aflatoxin B_1 and selected chemical carcinogens will be determined. The level of dietary protein will be the primary nutrition model employed and AFB_1 the primary carcinogen used in these studies.

Identifying number: R01 CA 20136
Principal investigator: Randall Wood
Institution: Texas Agricultural and Mechanical University
Title: Tumor Lipids: Metabolism and Structural Studies

Total FY79 obligation: $69,689
Nutrition allotment: 100%
Nutrition funding: $69,689

Total FY80 obligation: $66,158
Nutrition allotment: 100%
Nutrition funding: $66,158

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

This research is a continuation of investigations with minimal deviation hepatomas that have demonstrated the existence of a number of differences in the structure and metabolism of lipids relative to normal liver. The detailed characterization of the individual lipid classes at the molecular species level will be extended to plasma membranes and organelle fractions to determine which subcellular structures are affected. The origin of hepatoma lipids will be examined in a number of ways. Lipid requirements and the effects of various lipids on the growth and morphology of cultured hepatoma cells will be examined.

The relationship between the lipids of the host's circulation system and a solid host-grown hepatoma will be studied in the intact animal and the perfused hindquarters bearing hepatomas. These data will indicate to what extent the hepatoma depends on lipids derived from the host organism. Lipid metabolism studies will be carried out with cultured hepatoma cells, hepatocytes isolated from normal liver, and the host-grown hepatoma with the use of various labeled substrates to determine what lipids the hepatoma can synthesize. A comparison of the data will also indicate errors in biosynthesis or catabolism, loss of enzyme specificities, differences in turnover rates, and differences in metabolic routes between the normal and neoplastic hepatocytes. Data from all the proposed experiments will indicate: 1) the dependence and independence of the hepatoma on the lipids from the host's circulation system; 2) differences in lipid structure and metabolism between hepatomas and normal liver; and 3) the effect of dietary lipids on the growth and lipid metabolism of the hepatoma. These data will permit the evaluation of the therapeutic potential of controlling lipid metabolism in neoplasms as a means of controlling their growth.

Identifying number: R01 CA 20236
Principal investigator: Rolando Armijo
Institution: University of California, Los Angeles
Title: Epidemiology of Stomach Cancer and Nitrates in Chile

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This is a grant to puruse epidemiologic studies in Chile on the association between nittrate exposure and stomach cancer mortality and, within a broader context, to test the hypothesis that *N*-nitroso compounds may be carcinogenic for man. A previous study demonstrated a correlation between nitrate exposure and stomach cancer mortality in Chile. The present study is designed to meet three major objectives: 1) to determine whether a significant difference in exposure to variables indicative of a high nitrate intake exists in Chile between two groups of stomach cancer patients and their ill and well controls; 2) to explore for additional factors which might be of significance, other than cumulative nitrate exposure demonstrated in the previous correlation study; 3) to determine whether a correlation exists between nitrate/nitrite

Epidemiology of Stomach Cancer and Nitrates in Chile (continued)

exposure indicators and stomach cancer in low case-control and a nitrate ecology study being conducted concurrently during a 24-month period. The case-control study is using a questionnaire which covers many dietary factors and use of alcohol. As of December 31, 1977, 594 persons had been interviewed by the professional field investigators prior to knowledge of diagnosis. About one-sixth of those interviewed has a subsequent diagnosis of stomach cancer. It is expected that the 1,500 interviews (500 cases and 1,000 controls) will be completed by December 1978.

Identifying number: R01 CA 20695
Principal investigator: Adelbert E. Wade
Institution: University of Georgia
Title: Diet and Chemical Carcinogenesis

Total FY79 obligation: $38,797
Nutrition allotment: 100%
Nutrition funding: $38,797

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objective of this research is to determine the effects of selected dietary states on the function of drug-metabolizing enzymes of rat liver, lung, and intestinal mucosa. An evaluation will be made of changes in the rate of metabolism or the metabolic pathway of benzo[*a*]-pyrene, 2-acetylaminofluorene or dimethylnitrosamine with the potential to induce reverse mutations in histidine-dependent *Samonella typhimurium*. Verification of mutagenicity as a measure of carcinogenicity will be further correlated with the characteristics of binding of metabolites to calf thymus DNA.

Rats will be fed diets deficient in or supplemented with essential fatty acids or thiamin for 1 to 3 weeks. Metabolism of carcinogens will be assessed with the use of an in vitro microsomal system containing necessary cofactors or isolated perfused liver. Mutagenicity will be assessed with the use of the bacterial mutagenicity method developed by Ames. Various metabolites will be extracted from incubation or perfusion mixture with the use of thin-layer, high-pressure liquid and/or gas-liquid chromatography.

Identifying number: R01 CA 20709
Principal investigator: Richard A. Gams
Institution: University of Alabama, Birmingham
Title: Cellular Incorporation of Vitamin B_{12}

Total FY79 obligation: $42,041
Nutrition allotment: 100%
Nutrition funding: $42,041

Total FY80 obligation: $45,207
Nutrition allotment: 100%
Nutrition funding: $45,207

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The purpose of this investigation is to define the mechanism by which vitamin B_{12} is incorporated by mammalian cells. In vitro experiments will be performed with isolated rat ileal and hepatic cells, murine leukemia cells, and hamster embryo cells both before and after neoplastic transformation. With the use of purified B_{12}-transport proteins, B_{12} incorporation and processing by whole cells and isolated subcellular compounds will be studied.

Similarities and differences will be examined in uptake mediated by intrinsic factor, transcobalamin II and R-binders of B_{12} in normal and neoplastic cells to further our understanding of B_{12} transport and possibly to help define the role of B_{12} in mammalian cellular metabolic functions.

Identifying number: R01 CA 20807
Principal investigator: Frederick C. Kauffman
Institution: University of Maryland, Baltimore
Title: Pharmacology of Carcinogen Activation in Intact Cells

Total FY79 obligation: $49,716
Nutrition allotment: 10%
Nutrition funding: $4,972

Total FY80 obligation: $64,409
Nutrition allotment: 10%
Nutrition funding: $6,441

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Pharmacology of Carcinogen Activation in Intact Cells (continued)

Project description:

The long-term goal of this work is to characterize factors affecting the activation of carcinogens via mixed-function oxidase systems in intact cells. Initial studies will be done with the use of the isolated hemoglobin-free perfused rat liver as a model tissue in which the production of oxidized drug metabolites will be continuously monitored and correlated with changes in steady-state levels of key intermediates of energy metabolism and with the oxidation-reduction state of pyridine nucleotides, flavins, and cytochromes measured by tissue-surface fluorescence and absorbancy. Rates of mixed-function oxidation will be experimentally manipulated by exposure of animals to inducing agents, metabolic inhibitors, and altered nutritional states.

Information gathered in these studies will be used to identify metabolic events associated with the regulation of rates of mixed-function oxidation in intact hepatocytes. In order to gain insight into mechanisms generating NADPH, an obligatory substrate for mixed-function oxidation, substrates in equilibrium with this cofactor will be measured in extracts of livers freeze-clamped during the course of mixed-function oxidation. In addition, the effect of inducing agents and dietary alterations on enzyme activities associated with the generation of NADPH will be examined.

During the course of this work, methods will be developed to continuously monitor the metabolism of several carcinogens in perfused organs. In addition, experiments will be conducted to describe interactions between intermediary metabolism and carcinogen activation in several tissues, including rat liver, livers from mice which differ in their susceptibility to selected carcinogens, and lung. Knowledge gained in these studies may be ultimately applied to experimentally manipulating the incidence and rate of chemical carcinogenesis in laboratory animals.

Identifying number: R01 CA 20850
Principal investigator: David E. Ong
Institution: Vanderbilt University
Title: Cancer and Vitamin A

Total FY79 obligation: $40,383
Nutrition allotment: 100%
Nutrition funding: $40,383

Total FY80 obligation: $95,260
Nutrition allotment: 100%
Nutrition funding: $95,260

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The goal of this research is to contribute to the understanding of the means by which vitamin A exerts a prophylactic and therapeutic effect on certain experimental and spontaneous neoplasia. The research is designed to investigate and define what appear to be fundamental differences in the way vitamin A is handled by normal and neoplastic tissue, with particular attention to cellular binding proteins for vitamin A. This information may well suggest which cancers would be candidates for vitamin A therapy.

Identifying number: R01 CA 20897
Principal investigator: Laurence N. Kolonel
Institution: University of Hawaii
Title: Dietary Components and Cancer Development

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This study will correlate group-average dietary intake data, acquired over 2 years on a representative sample of 6,000 Oahu residents of Caucasian, Japanese, Chinese, Filipino, and Hawaiian ancestry, with the local race, age, and sex specific incidence rates for various sites of cancer. Dietary information will be obtained by personal interview, with the use of a pretested questionnaire and colored photographs to help establish quantitative intake. For its representative sample of the population, the study will take advantage of the Health Surveillance Program of the Hawaii Department of Health, which each year identifies a cluster sample of 5,000 households throughout the state. Race, sex and age specific incidence rates for cancer will be provided by the Hawaii Tumor Registry, a member of the SEER program.

Identifying number: R01 CA 20907
Principal investigator: Homer S. Black
Institution: Baylor College of Medicine
Title: Effects of Dietary Factors on UVL-Carcinogenesis

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The predisposition of experimental animals receiving high levels of dietary fat to certain types of chemically induced cancers is well established. However, the measure of response evoked by different types of fats appears to be related to factors other than degree of saturation. Similarly, the role of dietary cholesterol in ultraviolet light (UVL) carcinogenesis seems clouded by variations in diet not properly controlled in earlier studies. The involvement of dietary cholesterol in actinic skin cancer was suggested over 40 years ago, and recent evidence increases concern over the role of this natural sterol in UVL-carcinogenesis. It is planned to 1) evaluate the effect of nutritional stress factors, i.e., high cholesterol and quantitative and qualitative alterations in dietary fat, upon the incidence of UVL-induced skin cancer; and 2) determine whether dietary antioxidants have a moderating effect upon potential predisposition to carcinogenesis by dietary lipids.

Identifying number: R01 CA 20908
Principal investigator: Raymond R. Brown
Institution: University of Wisconsin, Madison
Title: Effect of Fat Saturation on Cancer Incidence in Mice

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

Animal feeding studies (mice) are under way to evaluate the effect of type of fat (degree of saturation) and quantity of fat in the diet (two levels) on the incidence of spontaneous and induced cancer in mice. Additional studies will test the effect of a diet high in trans isomers and high in triene content on cancer incidence. High-fat diets will also be fed with and without an antioxidant to evaluate this. Dietary substitutions are made on an isocaloric basis so that per calorie consumed, all other nutrient intakes will be constant. Ancillary studies will be done to evaluate the effects of these dietary manipulations on structure and functions of cellular components such as membranes, mitochondria, and microsomes.

Identifying number: R01 CA 20938
Principal investigator: Roslyn B. Alfin-Slater
Institution: University of California, Los Angeles
Title: Nutritional Stress on Aflatoxin-Induced Carcinogenesis

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Use of oral contraceptives is associated with changes in the metabolism of fat, proteins, and carbohydrates in the liver. This study is designed to investigate the possibility that oral contraceptives may alter resistance to toxicity by aflatoxin, a powerful liver carcinogen. Variations in tumor formation and growth will be studied in animal models.

Identifying number: R01 CA 20948
Principal investigator: James D. Yager, Jr.
Institution: Dartmouth College
Title: Effect of Dietary Stress on Pancreatic Carcinogenesis

Total FY79 obligation: $128,194
Nutrition allotment: 100%
Nutrition funding: $128,194

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Nutrition/Cause and Prevention

Effect of Dietary Stress on Pancreatic Carcinogenesis (continued)

Project description:

The incidence of human pancreatic carcinogenesis in the United States is rising. Recent epidemiologic data indicate that this disease may be of environmental etiology. The relationship of diet and nutrition to the etiology of several chemically induced cancers in experimental animal studies has been investigated. No studies for such a relationship to pancreatic cancer have been reported.

The recently developed azaserine model for pancreatic carcinogenesis in the rat will be used to investigate the effects of several dietary regimens. The dietary stresses in these initial screening studies are low-protein diet (9 percent), high-protein diet (50 percent), low-fat (5 percent) and high-fat (30 percent) diets of both saturated fats and polyunsaturated fats, and lipotropic-deficient diets. Animals in these studies will be injected with a carcinogenic regimen of azaserine and killed at 1 year for histopathologic evaluation.

On the basis of the results of these screens for the relationship of diet to the etiology of chemically induced pancreatic cancer, more definitive dietary studies and selected biochemical studies of the underlying mechanisms will be undertaken in the second year.

Identifying number: R01 CA 20960
Principal investigator: Christopher P. Holroyde
Institution: Lankenau Hospital
Title: Metabolic Study of Adult and Pediatric Cancer Patients

Total FY79 obligation: $155,478
Nutrition allotment: 100%
Nutrition funding: $155,478

Total FY80 obligation: $165,574
Nutrition allotment: 100%
Nutrition funding: $165,574

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The objective of this research is to investigate glucose and lactate metabolism in patients with malignant solid tumors, particularly colorectal cancer. With the use of isotope tracer infusion techniques, the production, utilization, and oxidation of glucose and lactate will be measured under standardized conditions. The possible relationship between lactate production and tumor growth will be investigated by observations on the effect of cancer therapy on lactate metabolism. In addition, the host metabolic response to nutritional supplementation by short-term intravenous hyperalimentation will be evaluated in debilitated patients.

Identifying number: R01 CA 20969
Principal investigator: Raoul Carubelli
Institution: Oklahoma Medical Research Foundation
Title: Sialoglycoconjugates in Cancer Under Dietary Stress

Total FY79 obligation: $40,349
Nutrition allotment: 100%
Nutrition funding: $40,349

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The chemistry and metabolism of membrane-bound and circulating sialoglycoconjugates will be investigated during chemical carcinogenesis in rats subjected to nutritional stress. The development of hyperplastic nodules and hepatomas induced in male rats by treatment with 2-acetylaminofluorene will be modulated by the level and degree of unsaturation of dietary lipids both in the presence and in the absence of added antioxidants.

The chemical studies will be designed to investigate the properties, chemical composition, and structure of sialic acid-rich glycoproteins. The studies will focus mainly on the enzymes responsible for the activation, transfer, and hydrolysis of sialic acids (i.e., CMP-NANA synthetase, sialyl transferase, and neuraminidase). These studies will be conducted with the use of serum and various membrane fractions from liver of normal, preneoplastic, and cancer-bearing rats.

The principal aims of this research are 1) to elucidate the molecular alterations of membrane-bound and circulating sialoglycoproteins, 2) to define the enzymatic derangements underlying these alterations, and 3) to establish the effect of the nutritional stress on these biochemical parameters in rats undergoing chemical carcinogenesis.

Identifying number: R01 CA 20990
Principal investigator: Russell O. Sinnhuber
Institution: Oregon State University
Title: Protein Effects of Aflatoxin Carcinogenesis in Trout

Total FY79 obligation: $68,636
Nutrition allotment: 100%
Nutrition funding: $68,636

Total FY80 obligation: $61,508
Nutrition allotment: 100%
Nutrition funding: $61,508

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The rainbow trout (Salmo gairdneri) will be used to study the effects of dietary protein on hepatocellular carcinoma (hepatoma) induction and development. Aflatoxin B_1, a useful secondary carcinogen yielding consistent results in laboratory animals, will be used to induce neoplasia in the fish. Rainbow trout are the most sensitive known experimental animals as regards carcinogenic properties of AFB_1 and are similar to humans and nonhuman primates in their in vitro metabolic conversion of AFB_1. This model provides a convenient test system in which to determine the effects of diet on tumor induction and growth. In addition, exposure of the trout eggs to AFB_1 for a short time yields a population of latent cancer-bearing animals in which dietary factors can be evaluated.

The effects of dietary protein on AFB_1 carcinogenesis and biochemical mechanisms through which these effects are exerted will be investigated by combining in vivo studies of tumor production in trout with in vitro studies on the enzymatic activation and detoxification of AFB_1, identification and quantification of AFB_1 metabolites, and conversion of AFB_1 to active bacterial mutagens.

Identifying number: R01 CA 20997
Principal investigator: Daniel W. Nixon
Institution: Emory University
Title: Metabolic Study of Cancer Patients

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The overall objective of this project is to develop and apply quantitative methods for evaluating the effects of hyperalimentation (HA) in the undernourished cancer patient. Answers to the following questions are being sought: 1) Can cancer undernutrition be corrected by HA, and which method, parenteral or enteral, is most effective? 2) What is the effect of HA on neoplastic growth? Biochemical and radiological parameters of tumor activity are being monitored in a serial fashion. 3) What is the effect of HA on chemotherapy side effects? Both subjective and objective adverse effects are being evaluated. 4) What is the effect of chemotherapy on metabolic repletion by HA? Metabolic balance studies are being performed before, during, and after HA and chemotherapy.

Identifying number: R01 CA 20998
Principal investigator: John A. Schmitz
Institution: Oregon State University
Title: Mammary Tumors: Dietary Fatty Acids/Selenium Effects

Total FY79 obligation: $74,509
Nutrition allotment: 100%
Nutrition funding: $74,509

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The influence of dietary fat types, individual dietary fatty acids, and possible dietary fat-selenium interactions on development of spontaneous mammary tumors in virgin female C3H mice is being studied.

This is being done by including, as 10 percent of the total diet, fats from various sources, singularly and in computerized combinations, to yield the lowest possible correlation ratios between fatty acids. Additional groups of mice are fed diets representing plant or animal fats or various degrees of fatty acid saturation and supplemented with 2 ppm sodium selenite in the drinking water.

Feed consumption is being measured and the mice are weighed and palpated for mammary tumor development weekly. Rate of tumor growth is recorded. Tissues from mice in each dietary group are analyzed for lipid and selenium content and glutathione peroxidase activity.

Identifying number: R01 CA 20999
Principal investigator: Walter Troll
Institution: New York University
Title: Fat Level and Saturation in Carcinogenesis

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Epidemiological studies indicate that the major source of human cancer is of environmental origin and is related to dietary habits. The effects of unsaturated and saturated fats on mouse skin are being assessed by feeding synthetic diets to mice throughout the initiation and promotion process. Groups of 30 mice were initiated with 30 mg beta-propiolactone and 25 micrograms DMBA. They were put on diets containing saturated and unsaturated fat at two levels: 4 percent and 15 percent. All groups were treated three times a week with 5 mg phorbol myristate acetate as tumor promoter. There was a strikingly greater tumor yield after 3 months on the polyunsaturated diets. On the 15 percent fat diet, BPL-initiated mice on the unsaturated diet showed 22 tumors, while the animals on saturated fat showed 4 tumors. With the DMBA-initiated group the animals on the unsaturated diet showed 122 tumors, and 21 on the saturated diets. The following tentative conclusions can be drawn from this experiment: 1) unsaturated fat enhances the action of the tumor promoter PMA; 2) unsaturated fat has the same effect on DMBA initiation as PBL; thus, it is not involved in the activation of the carcinogen DMBA, which requires activation; and 3) the proximal agent of unsaturated fat in this process requires investigation. Possible candidates are malonaldehyde, prostaglandins, or epoxides. Experiments are planned to delineate further the effect of diet on initiation and promotion by using unsaturated fat during initiation, switching to saturated during promotion, and vice versa. The saturation of skin lipids will be measured.

Identifying number: R01 CA 21007
Principal investigator: Joseph L. Lyon
Institution: University of Utah
Title: Diet and Colon Cancer in a Low-Risk Population

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The incidence of colon cancer in Utah is 30-35 percent below U.S. rates. Important risk differences by place of residence and religion are also present in the Utah population. A case-control study will be done to explore the effect of diet on these unusual risk factors. Cases of colon cancer will be identified and a population control chosen. Extensive dietary information will be obtained through interviews. Dietary items will be analyzed by their nutrient components for elements associated with colon cancer such as high fat intake.

Identifying number: R01 CA 21019
Principal investigator: Paul B. McCay
Institution: Oklahoma Medical Research Foundation
Title: Dietary Fats and Antioxidants in Carcinogenesis

Total FY79 obligation: $125,851
Nutrition allotment: 100%
Nutrition funding: $125,851

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The major objective is to investigate 1) the dietary content of high saturated fat, high unsaturated fat, or low fat; 2) the stress caused by a lack of antioxidant content in the diet; and 3) the tumorigenic action of two different carcinogens. The diets used will have either high or low fat content, and antioxidants will be either present or absent.

Although high-fat diets have been demonstrated to enhance tumorigenesis by certain carcinogens and diets supplemented with antioxidants have been reported to depress carcinogenesis by such compounds, the relationship between these phenomena has not been studied. This appears well worth investigating, since ample information suggests that peroxidative reactions of lipid may be involved in the promotion of tumor formation initiated by carcinogens.

Dietary Fats and Antioxidants in Carcinogenesis (continued)

The protective action of antioxidants against a number of carcinogens may be due to their capacity to inhibit lipid peroxidation. If this is the case, an antagonistic effect should be observed in animals fed diets high in polyunsaturated fat, i.e., antioxidant supplementation may be less effective in this group than in the other dietary groups in depressing tumor incidence.

The animals fed the polyunsaturated-fat diet deficient in antioxidants might be expected to develop a greater incidence of tumors earlier than animals fed antioxidant-deficient diets containing saturated fat or very little fat. On the other hand, the protective action of dietary antioxidants against carcinogenesis may be related to possible induction of certain drug-metabolizing enzymes that could then influence metabolism of carcinogens. The project is designed to obtain information which will indicate whether or not either or both of these mechanisms are operating.

Identifying number: R01 CA 21020
Principal investigator: Shiang P. Yang
Institution: Texas Tech University
Title: Effect of Lipids on Metabolism of Chemical Carcinogens

Total FY79 obligation: $55,680
Nutrition allotment: 100%
Nutrition funding: $55,680

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objectives of this study are 1) to study the effect of dietary lipids on the metabolic activation of chemical carcinogens, and 2) to correlate the enzyme activities of the liver and mammary gland with the neoplastic development.

Tallow, corn oil, and coconut oil will be used as the dietary lipids and *N*-2-fluorenylacetamide (FAA) as the chemical carcinogen. Male and female weanling rats will be fed ad libitum for 6 months an otherwise adequate but lipid-free diet supplemented with the above lipids. From the 2nd to the 5th month, 20 animals in each dietary group will receive the experimental diet supplemented with FAA while the remaining 10 animals will continue to receive the FAA-free diet.

Both the experimental and control groups will receive the FAA-free diets during the 6th month. At the end of the experiment, the carcinogenesis in the liver and mammary gland will be studied. The enzyme activity of the S-9 and S-150 fractions of the liver and mammary gland will be determined by the in vitro production of ultimate mutagen(s) with a bacterial tester system or by other physical-chemical procedures.

Identifying number: R01 CA 21104
Principal investigator: James E. Trosko
Institution: Michigan State University
Title: Mutation and Derepression of Genes in Carcinogenesis

Total FY79 obligation: $135,872
Nutrition allotment: 10%
Nutrition funding: $13,587

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This is primarily an in vitro somatic cell genetic analysis of human cells. The modulation of DNA mutation frequencies and DNA repair frequencies by environmental factors will be studied. DNA damage will be induced, in part, by caffeine.

Identifying number: R01 CA 21157
Principal investigator: Emmanuel Farber
Institution: University of Toronto
Title: Pathogenesis of Liver Cancer Induced by Chemicals

Total FY79 obligation: $62,060
Nutrition allotment: 10%
Nutrition funding: $6,206

Total FY80 obligation: $33,245
Nutrition allotment: 10%
Nutrition funding: $3,325

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Pathogenesis of Liver Cancer Induced by Chemicals (continued)

Project description:

This grant includes study of the biochemical, morphologic biochemical basis for the development of liver cancer induced by diethylnitrosamine, 2-acetylaminofluorene, dimethylnitrosamine, and other hepatic carcinogens.

Identifying number: R01 CA 21258
Principal investigator: Edward Bresnick
Institution: University of Vermont and State Agricultural College
Title: In Vivo-In Vitro Model for Identification of Carcinogens

Total FY79 obligation: $74,306
Nutrition allotment: 10%
Nutrition funding: $7,431

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Nitrosamines, among other carcinogens, will be used to develop a host-mediated in vitro model for the identification of potential carcinogens. The cell will be examined for various markers of transformation and the ease of malignant transformation will be established.

Identifying number: R01 CA 21359
Principal investigator: John S. Bertram
Institution: Roswell Park Memorial Institute
Title: Cell Interactions During Malignant Transformation

Total FY79 obligation: $32,180
Nutrition allotment: 100%
Nutrition funding: $32,180

Total FY80 obligation: $65,770
Nutrition allotment: 100%
Nutrition funding: $65,770

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

It has recently been found in this laboratory that the expression of the malignant phenotype in the C3H/10T1/2CL8 assay system for malignant transformation can be repressed by high levels of serum. This repression can be reversed by exposure to suboptimal concentrations of serum. This proposal is concerned with the mechanisms whereby the expression of the malignant phenotype can be modified.

The project is divided into two stages: 1) an investigation of other selective media for the transformed phenotype; specifically, it is proposed to investigate the effects of suboptimal concentrations of isoleucine and of calcium; and 2) an investigation of the mechanisms whereby expression of the malignant phenotype can be inhibited or enhanced. In stage 1, concentrations of isoleucine and of calcium will be chosen which cause a restriction in growth rate of normal but not of transformed cells. Carcinogen-treated cultures will then be exposed to the selective procedure at various times after treatment, and the rate of development and number of transformed foci measured.

In stage 2 of this project, the mechanisms of the effects of selective medium (serium, isoleucine, calcium) will be studied in carcinogen-treated cultures containing latently transformed cells, in reconstruction experiments utilizing mixed cultures containing latently transformed cells, and in reconstruction experiments utilizing mixed cultures of normal and transformed cells. Two questions will be asked. 1) Is the observed effect due to cell/cell interaction, i.e., can normal cells repress the expression of malignancy in transformed cells? This will be approached by adding cells and cell products to cultures in which expression is maximal. 2) Is the observed effect mediated via cyclic nucleotides? This will be approached by the addition of exogenous dibutyryl cyclic AMP and dibutyryl and cyclic GMP, and by the use of drugs which stimulate the synthesis (prostaglandin E_1), or retard the degradation of cyclic AMP (1-methyl-3-isobutyl xanthine), or which elevate cyclic GMP levels and depress cyclic AMP levels (insulin).

Identifying number: R01 CA 21419
Principal investigator: Paul B. McCay
Institution: Oklahoma Medical Research Foundation
Title: Chemical Carcinogenesis in Specific Dietary States

Total FY79 obligation: $15,692
Nutrition allotment: 100%
Nutrition funding: $15,692

Chemical Carcinogenesis in Specific Dietary States (continued)

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The influence of the amount and degree of unsaturation of dietary fat on tumor production by carcinogens and how the presence or absence of antioxidant in these same diets affects the tumor incidence will be investigated. Preliminary studies indicate that the inhibitory effect of antioxidants on chemical carcinogenesis promoted by dietary fat may be related to the property of antioxidants for inhibiting peroxidation of unsaturated fat.

The studies in this project are designed to probe these interrelationships more deeply. The preliminary studies will be repeated for confirmation. Several antioxidants and carcinogens will be tested. It will then be determined if consumption of dietary antioxidant is required only for a short time before, during, or after treatment with a carcinogen, or if long-term maintenance of the animals on the antioxidant-containing diet is required to ensure reduced tumor incidence.

In addition, studies will be done on the effect of feeding the various diets on the capacity of microsomes to form mutagenic compounds in vitro from the carcinogens to be studied, since modulation of the system which metabolizes carcinogens may be induced by the different diets. The metabolism of the carcinogens by primary liver-cell cultures and microsomes from animals on the different diets for evidence of production of reactive carcinogen free radicals will be studied with the use of the electron spin resonance (ESR) spin-trapping technique developed in this laboratory for detecting enzyme-generated radicals.

An investigation is planned to determine the capacity of certain carcinogens to initiate lipid peroxidation in microsomes and primary liver-cell cultures from animals fed the different diets to determine if this property can be related to the metabolism of the carcinogen to free radical forms and to the inhibitory effect of antioxidants on tumorigenesis. Finally, studies will be done on the distribution and retention time of ^{14}C-labeled carcinogens in various tissues of animals fed the different diets with and without antioxidants. The fraction of the ^{14}C-label in selected tissues that is acetone soluble and acetone insoluble will be determined.

Identifying number: R01 CA 21514
Principal investigator: Michel A. Ibrahim
Institution: University of North Carolina, Chapel Hill
Title: Assessment of Past Diet in Cancer Epidemiology

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The need for a reliable method for estimating dietary consumption in the past has become critical in case-referent epidemiological studies of the relationship of diet to cancer. The research objective of this study is to estimate the reliability of estimates of past dietary intake which are derived from present diet histories or from retrospective diet histories. A population on which a current diet history was performed in 1960 is located in Evans County, Georgia. This population will be reinterviewed about their recollections of their diet in 1960, and their current diet in 1978. The reliability of the retrospective diet history will be assessed by comparing it to the diet history obtained in 1960. The reliability of the current diet history as an index of past dietary intake, as well as the degree of dietary change in this population in 18 years, will be assessed by comparing the 1978 current diet history to the 1960 history. Rigorous evaluation of the available methods for assessing past diet is needed. This study will contribute to a quantitative estimate of their value. Should their reliability prove low, waste of resources on unreliable studies will be avoided. Should their reliability prove high, studies will not fail to be undertaken because of unwarranted negative prejudice against these methods.

Identifying number: R01 CA 21617
Principal investigator: Leland L. Smith
Institution: University of Texas Medical Branch, Galveston
Title: Potentially Carcinogenic and Atherogenic Sterols

Total FY79 obligation: $39,898
Nutrition allotment: 100%
Nutrition funding: $39,898

Total FY80 obligation: $1,130
Nutrition allotment: 100%
Nutrition funding: $1,130

Potentially Carcinogenic and Atherogenic Sterols (continued)

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Examination of naturally aged cholesterol batches for their inherent mutagenicity towards test strains of *Salmonella typhimurium* will be continued. Naturally aged cholesterol is mutagenic towards several such strains, and this project is designed to determine which autoxidation products account for this biological activity. Fractionation of aged cholesterol preparations will be continued and such fractions will be assayed for mutagenicity until active subfractions are identfied.

Individual mutagenic sterols will be sought, their chemical identities established, and a thorough evaluation of their mutagenicities towards the bacterial strains made. Mutagenicity towards other test systems may also be studied. Mutagenic sterols will be isolated by means of high-performance liquid-column chromatography, their identities established by chromatographic, spectral, and chemical evidence.

Identifying number: R01 CA 21663
Principal investigator: Edgar C. Henshaw
Institution: University of Rochester
Title: Intermediary Metabolism in Animals and Humans

Total FY79 obligation: $176,521
Nutrition allotment: 100%
Nutrition funding: $176,521

Total FY80 obligation: $185,242
Nutrition allotment: 100%
Nutrition funding: $185,242

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The goal of this work is the elucidation of the mechanisms controlling the rate of protein synthesis at the cytoplasmic level in mammalian cells. The tissue utilized in the present studies is the Ehrlich ascites tumor cell growing in suspension culture. This cell demonstrates cytoplasmic control mechanisms which respond vigorously to alterations in nutrient (essential amino acid, glucose, or serum) concentration in the medium.

Upon nutrient deprivation, one such mechanism operates to inhibit polypeptide chain initiation by inhibiting the formation of the initiation complex consisting of the native 40 s ribosomal subunit plus bound Met-tRAF, the initiating aminoacyl tRNA. Formation of this complex requires the Met-tRNAF binding factor, GTP, Met-tRNAF, and an active native 40 s subunit. These components are being examined to determine which is modified during nutrient deprival. Current studies are focused on an inhibitor of this reaction which is present in Ehrlich cells and which appears, like the hemin-controlled reticulocyte inhibitor, to phosphorylate the smaller subunit of the Met-tRNAf binding factor.

Identifying number: R01 CA 21705
Principal investigator: Curtis Harper
Institution: University of North Carolina, Chapel Hill
Title: Lung Toxicity to Environmental Organohalogens

Total FY79 obligation: N/A

Total FY80 obligation: $71,592
Nutrition allotment: 5%
Nutrition funding: $3,580

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The pulmonary toxicity of some environmental organohalogens is well established while some others are strongly suspected of having pulmonary toxicity. The objective of this research is to show that some organohalogen compounds induce lesions in the lung more readily than they do in the liver, in part because of the relatively low aldehyde dehydrogenase activities in pulmonary tissues. We will show direct correlations between the biotransformation of organohalogens to aldehydes and pulmonary injury. It will also be shown that the aldehyde intermediates of many of these agents are formed in the liver, since the lung is also deficient in alcohol dehydrogenases. Changes in activities of some pulmonary enzymes will be established as biochemical indices of pulmonary injury.

Trichloroethylene, halogenated ethers and 2-chloroethanol have been selected as primary compounds in this investigation because they are established environmental toxicants with widely different chemical properties. Biotransformation to aldehydes is one of the few common properties of all these agents.

The relationship between biotransformation to aldehydes and pulmonary toxicity will be established by 1) pretreatment with drugs which change the balance of active intermediates in organohalogen metabolism;

Lung Toxicity to Environmental Organohalogens (continued)

2) studying the accumulation of aldehyde intermediates in lung and assessing the potential of these intermediates to initiate toxic reactions by covalent binding or lipid peroxidation; 3) comparing the pulmonary toxicities to other organohalogens with similar chemical properties that are not converted to aldehydes; and 4) studying the organohalogen toxicities in animals maintained on restrictive diets, all of which are known to influence toxicity/carcinogenicity but only some of which are known to influence biotransformation.

Identifying number: R01 CA 21857
Principal investigator: Atif B. Awad
Institution: Kirksville College of Osteopathic Medicine
Title: Role of Fatty Acids in Membrane Functional Properties

Total FY79 obligation: $21,658
Nutrition allotment: 100%
Nutrition funding: $21,658

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The incorporation of elaidic acid into Ehrlich ascites tumor cells (EATC) upon feeding the host an elaidic acid-rich diet has been investigated. The EATC lipids contained only one-half the concentration of elaidic acid found in the lipids of either the host livers or livers from normal mice. On the other hand, elaidic acid incorporation into tumor cells was close to that of ascites fluid. This incorporation was mainly into phospholipids; the highest into choline phospholipids and ethanolamine phospholipids. EATC phospholipids had reduced polyunsaturated fatty acids as compared with oleic acid-grown cells. Tumor development was accompanied by an increase in elaidic acid of the host's liver. Only in EATC did elaidic acid incorporation in tissues studied result in a reduction in the amount of all major lipids in the tumor. The development of the tumor did result in decreases in triacylglycerols and esterified cholesterol and in increases in phospholipids and free cholesterol in the livers of host animals.

Identifying number: R01 CA 22077
Principal investigator: Donald P. D'Amato
Institution: University of Connecticut Health Center
Title: Zinc Radiopharmaceuticals for Ocular Melanoma Detection

Total FY79 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Cancer activity/thrust: Diagnostic Research/Detection and Diagnosis

Project description:

The investigation of the practicality of zinc radiopharmaceuticals for noninvasive ocular melanoma detection is the objective of this work. Naturally high levels of zinc within uveal tissues and the known association of zinc with melanin combine to form the rationale for the application of zinc compounds. In this project ^{65}Zn and radiopharmaceuticals presently used for melanoma localization will be injected into animals and the uptake ratio between cancerous and normal ocular tissues measured. The effect on uptake of the chemical complex of zinc, of the site and time of injection, and of the dietary content of natural zinc will be investigated. Natural zinc stores within normal and neoplastic tissue will be measured by atomic absorption analysis and x-ray fluorescence methods.

Identifying number: R01 CA 22183
Principal investigator: George E. Gifford
Institution: University of Florida
Title: Nutritional Aspects of Vitamin A and Cancer

Total FY79 obligation: $55,959
Nutrition allotment: 100%
Nutrition funding: $55,959

Total FY80 obligation: $61,539
Nutrition allotment: 100%
Nutrition funding: $61,539

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Nutritional Aspects of Vitamin A and Cancer (continued)

Project description:

Vitamin A and related compounds (retinoids) have been shown to have preventive and therapeutic effects on several types of tumors in the intact animal, to prevent carcinogen-induced hyperplasia in organ culture, and to restore some functions of normalcy to transformed cells in culture. Animals deficient in vitamin A are also more susceptible to carcinogens and may be more prone to development of spontaneous tumors.

The overall objective is to study the antitumor effects of retinoids, specifically, to study the effects of retinoids on tumor cells in culture: 1) to develop an in vitro model for the study of the direct effects of retinoids on tumor cell proliferation, 2) to study direct effects of retinoids on parameters of transformation, 3) to resolve the discrepancy in results of retinoid treatment on tumors grown in vivo and in vitro, and 4) to study the mechanism of action of retinoids on DNA synthesis and control of proliferation of tumor cells.

Identifying number: R01 CA 22209
Principal investigator: Paul D. Sullivan
Institution: Ohio University
Title: Antioxidant Interaction with Benzo[a]pyrene and Derivatives

Total FY79 obligation: $54,486
Nutrition allotment: 50%
Nutrition funding: $27,243

Total FY80 obligation: $54,105
Nutrition allotment: 50%
Nutrition funding: $27,053

Cancer activity/thrust: Carcinogensis/Cause and Prevention

Project description:

Certain antioxidants, such as BHA, a food additive antioxidant, are known to inhibit the production of cancers from polycyclic hydrocarbons in test animals. The mechanism of this inhibition is not fully understood. In this study the effects of various antioxidants and combinations of antioxidants on the in vitro metabolism of benzo[a]pyrene by rat liver microsomes will be examined.

Identifying number: R01 CA 22326
Principal investigator: Willard J. Visek
Institution: University of Illinois
Title: Dietary Protein-Fat Interactions in DMBA Mammary Cancer

Total FY79 obligation: $46,105
Nutrition allotment: 100%
Nutrition funding: $46,105

Total FY80 obligation: $48,063
Nutrition allotment: 100%
Nutrition funding: $48,063

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objective of this study is to determine how the quantities of two major dietary nutrients, protein and lipid, interact to influence 7-12 dimethylbenz[a]anthracene (DMBA) mammary carcinogenesis in rats. Different concentrations of dietary protein and lipid will be fed in casein-containing diets with the following milligrams of protein per kilocalorie of dietary energy: 20, 30, and 80. Lipid will be supplied as corn oil at 13, 26, and 54 mg/kilocalorie of dietary energy at each of three dietary levels of protein. Minerals, vitamins, and fiber will be supplied at a constant ratio per kilocalorie of dietary energy for all dietary treatments.

Experiments are designed to study dietary influences on the initiation and promotion phases of carcinogenesis. The absorption, tissue distribution, and excretion of DMBA and its metabolites will be determined. Binding of DMBA metabolites to RNA, DNA, and protein of mammary tissue will be studied. Metabolites in urine and feces will be identified and quantitated. Liver aryl hydrocarbon hydroxylase and related mixed-function oxidase components will be assayed to determine how the dietary variables influence their activity. All tumors will be studied histologically.

Identifying number: R01 CA 22410
Principal investigator: Maria C. Linder
Institution: California State University, Fullerton
Title: Copper Absorption and Ceruloplasmin in Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Copper Absorption and Ceruloplasmin in Cancer (continued)

Total FY80 obligation: $50,487
Nutrition allotment: 100%
Nutrition funding: $50,487

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

The objective of this research is to follow up on the observation that copper absorption is enhanced in tumor-bearing rats. This increase occurs in conjunction with other aberrations of copper metabolism in cancer, especially in elevated concentration and enhanced synthesis of the circulating copper protein, ceruloplasmin. Since so little is known about the basic mechanism of intestinal copper absorption and its regulation, this process will be studied first in normal rats, then in tumor-bearing animals.

In vivo and in vitro studies will be done with the use of ^{67}Cu and ^{64}Cu. The uptake and distribution of copper within the mucosa and its further transfer across the serosal surface will be studied. The influence of copper status and hormonal factors in the process of absorption will also be examined. It is expected that such studies will provide much basic information on the mechanism and regulation of copper absorption and explain the increased absorption which occurs in animals with tumors.

Identifying number: R01 CA 22524
Principal investigator: Donald R. Buhler
Institution: Oregon State University
Title: Metabolism and Toxicity of Pyrrolizidine Alkaloids

Total FY79 obligation: $59,753
Nutrition allotment: 100%
Nutrition funding: $59,753

Total FY80 obligation: $84,570
Nutrition allotment: 100%
Nutrition funding: $84,570

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This study is designed to establish whether a public health hazard results from consumption of meat and dairy products derived from livestock feeding on tansy ragwort (*Seneco jacobea*), a widely dispersed plant containing the hepatotoxic pyrrolizidine alkaloids. The toxicity of milk and tissue from cows and goats will be determined in feeding studies with rats.

This project will also study the absorption, excretion, distribution, and metabolism of senecifoline and jacobine, the two principal pyrrolizidine alkaloids from tansy ragwort, in two species of laboratory animals, the rat (susceptible) and the guinea pig (resistant), and in two species of lactating farm animals, the cow (susceptible) and the goat (resistant). Particular emphasis will be placed on isolating and characterizing reactive metabolites of the pyrrolizidine alkaloids, establishing whether covalent binding of such metabolites to tissue constituents occurs, and in establishing the mechanism(s) for toxicity of the alkaloids to mammals.

Identifying number: R01 CA 22609
Principal investigator: Gerhard Stohrer
Institution: Sloan-Kettering Institute for Cancer Research
Title: Purine Derivatives and Other Chemical Carcinogens

Total FY79 obligation: $74,972
Nutrition allotment: 100%
Nutrition funding: $74,972

Total FY80 obligation: $71,439
Nutrition allotment: 100%
Nutrition funding: $71,439

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The effect of various antioxidants on carcinogenesis in the rat will be studied. These will include food additives such as BHT. Attempts will be made to determine the mode of action of these carcinogenic inhibitors focusing on alterations in metabolic activation of carcinogens and alterations of cyclic nucleotide levels.

Identifying number: R01 CA 22683
Principal investigator: Peter M. Elias
Institution: University of California, San Francisco
Title: Antineoplastic Action of Vitamin A in Skin Cancer

Total FY79 obligation: N/A

Antineoplastic Action of Vitamin A in Skin Cancer (continued)

Total FY80 obligation: $32,684
Nutrition allotment: 100%
Nutrition funding: $32,684

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

Natural and synthetic retinoids offer exciting possibilities as epithelial cancer-preventing and cancer-treatment agents. Although their antineoplastic potency has been demonstrated in numerous animal models, their usefulness in human malignancy is only now being ascertained. Furthermore, the mechanism(s) whereby retinoids influence epithelial differentiation remains unknown. In this project we will be assessing the subcellular basis for the retinoids' activity against cancer, focusing on changes in membrane structures, particularly gap junctions, in microfilaments, and in the basement membrane in human basal cell carcinomas treated with topical retinoids. In addition, we wish to ascertain by clinical testing if the retinoids are clinically useful for the therapy of established basal cell cancers. Preliminary results indicate that retinoids stimulate a proliferation in the size and number of gap junctions in basal cell cancer cell membranes. Since gap junctions are important for intercellular communication and cell regulation, this may represent one possible mechanism for the retinoid's antineoplastic activity.

Identifying number: R01 CA 22717
Principal investigator: Barry Shane
Institution: Johns Hopkins University
Title: Regulation of Folate Poly-Gamma-Glutamate Synthesis

Total FY79 obligation: $55,540
Nutrition allotment: 100%
Nutrition funding: $55,540

Total FY80 obligation: $62,323
Nutrition allotment: 100%
Nutrition funding: $62,323

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

Folylpoly-gamma-glutamate synthetase will be purified from a variety of bacterial and mammalian sources, and its substrate specificity and kinetic properties will be examined to determine whether they are responsible for the different types of pteroylpolyglutamates found in various cell lines. Pteroylpolyglutamate substrates and potential analog inhibitors of the synthetase will be synthesized by a solid-phase procedure. The effects of products of one-carbon metabolism, such as methionine, thymidine, and adenosine, on the folate requirements, on the glutamate chain lengths of endogenous folates, and on folylpoly-gamma-glutamate synthetase levels will be examined in bacteria and in a variety of tumorigenic and nontumorigenic mammalian cells.

These studies will investigate whether one-carbon metabolism is controlled by varying the glutamate chain length of endogenous pteroylpolyglutamates and whether differences exist in folate requirements for products of one-carbon metabolism between normal and malignant cells.

Inhibitors of folylpoly-gamma-glutamate synthetase will be tested for their ability to cause cellular folate depletion by preventing the formulation of pteroylpolyglutamates, the forms of vitamin that are selectively retained by tissues.

Identifying number: R01 CA 22768
Principal investigator: James C. Smith
Institution: Florida State University
Title: Taste Aversion as a Factor in Cancer Therapy

Total FY79 obligation: $64,316
Nutrition allotment: 100%
Nutrition funding: $64,316

Total FY80 obligation: $66,934
Nutrition allotment: 100%
Nutrition funding: $66,934

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

Radiation-induced taste aversion in laboratory animals may serve as a model for taste aversions and subsequent anorexia observed in clinical radiation therapy patients. Since the typical radiation procedure used in animal studies differs in a number of important aspects from the exposure conditions employed in clinical situations, it is planned to study the formation of radiation-induced taste aversion in rats under treatment conditions that mimic clinical procedures.

This will involve taste aversion studies with multiple, low-dose, partial-body radiation exposures instead of the usual single, high-dose, whole-body irradiation procedures employed in animal studies.

Taste Aversion as a Factor in Cancer Therapy (continued)

Once the effects of these treatment parameters are established, techniques for blocking radiation-induced taste aversions in rats will be investigated. Specifically, the effects of different doses of antihistamines as well as food deprivation before and after irradiation will be studied to determine the optimal treatment regimen for blocking taste aversions.

It is hoped that these studies will suggest prophylactic measures which can be used in clinical radiation therapy. Since treatments such as antihistamine injections could compromise the clinical effectiveness of the radiation in destroying cancer cells, studies will be conducted to test for these effects.

In addition, extensive but noninvasive data collection will be initiated with human radiation therapy patients. Based on information obtained from hospital records, questionnaires, daily interviews, and diaries, an evaluation will be made of the incidence of dietary problems, in particular, changes in dietary habits, experienced by radiation therapy patients. The initial goal will be to determine whether some of the dietary problems encountered in clinical radiation therapy are the result of radiation-induced taste aversion.

Identifying number: R01 CA 22860
Principal investigator: Leo E. Gerweck
Institution: Massachusetts General Hospital
Title: Metabolic Factors in Heat and Radiation Lethality

Total FY79 obligation: $64,759
Nutrition allotment: 30%
Nutrition funding: $19,427

Total FY80 obligation: $71,484
Nutrition allotment: 30%
Nutrition funding: $21,445

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

The objective of this study is to determine the hyperthermic modifying effect of selected extracellular environmental conditions on cultured mammalian cells. The relationship between hyperthermic lethality and the following conditions will be examined: 1) oxygen tension, 2) hydrogen ion concentration, 3) nutritional deprivation, and 4) the interrelationship of these factors.

Specifically, the hyperthermic oxygen enhancement ratio will be determined and compared to the radiation oxygen enhancement ratio at selected oxygen concentrations. The response of cells to heat or radiation will be determined under acute and chronic hypoxic conditions. These experiments will be performed at selected elevated temperatures, 41-45°C. Variable oxygen tensions will be obtained with the use of a rapid gassing technique and low-density cultures to eliminate nutritional deprivation and change in pH. The response of cells at selected hydrogen ion concentrations to elevated temperatures or X irradiation will be determined under oxygenated and acute and chronic hypoxic conditions. Experiments will be designed to determine if nutritionally deprived plateau-phase cells are relatively sensitive to heat.

The results will be evaluated with respect to changes in age distribution, pH, oxygen tension, and nutritional history. Numerous observations have demonstrated that the concentration of extracellular metabolites in normal and tumor tissues varies significantly. The effect of these factors on hyperthermic lethality will be identified and quantitatively evaluated.

It is expected that the data obtained will provide a rationale for the use of hyperthermia to treat cancer which is based on naturally occurring differences between normal and tumor tissues.

Identifying number: R01 CA 22879
Principal investigator: A. David Goodman
Institution: Albany Medical College
Title: Role of Thyroid Hormones and Iodine in Breast Cancer

Total FY79 obligation: $55,493
Nutrition allotment: 50%
Nutrition funding: $27,747

Total FY80 obligation: $64,245
Nutrition allotment: 50%
Nutrition funding: $32,123

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

It has been suggested that hypothyroidism predisposes to the development of breast cancer in humans. However, studies concerning the effects of hypothyroidism on mammary cancer induced in rats by dimethylbenzathracene (DMBA) have yielded inconsistent results.

Role of Thyroid Hormones and Iodine in Breast Cancer (continued)

The overall objectives in this study are as follows: 1) to examine selectively the effects of hypothyroidism and of iodine deficiency on the induction and growth phases of DMBA-induced mammary carcinoma in the rat; 2) to study the mechanism of these effects; and 3) to examine the regulation of iodine metabolism and of conversion of thyroxine to triiodothyronine within the tumor, in relation to tumor growth.

It is planned to examine the effects of iodine deficiency with and without thyroxine replacement on DMBA-induced carcinogenesis. The effects of mild hypothyroidism induced by low doses of propylthiouracil will also be studied to avoid the decrease in food intake characteristic of severe hypothyroidism. Further, the effect of hypothyroidism induced prior to the administration of DMBA will be compared with that produced after DMBA administration. The effects of hypothyroidism on the prolactin and on the estrogen dependence of the tumors will also be examined.

Mammary tissue concentrates and organifies iodine, which indicates that iodine plays a role in its metabolism. The uptake of ^{131}I by DMBA-induced tumors will be studied, and the response of this process to oophorectomy and its relation to tumor growth will be examined. It will also be determined whether the DMBA tumor is one of the several tissues that can convert thyroxine to triiodothyronine, and the effect of oophorectomy on this process will be investigated. The production of T_3 within the tumor is of interest, because this hormone, through its demonstrated capacity to bind to receptors associated with nuclear DNA, could affect the rate of tumor growth.

Identifying number: R01 CA 22937
Principal investigator: Herschel Sidransky
Institution: George Washington University
Title: Effect of Nutritional Stress on Carcinogenesis

Total FY79 obligation: $19,364
Nutrition allotment: 100%
Nutrition funding: $19,364

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This project is designed to evaluate the effect of selected nutritional stresses (amino acid deficiencies, protein deficiency, high tryptophan diet, and alcohol) on the induction of liver cancer due to chemical carcinogens. The project will test whether alterations in diet may influence the incidence and course of development of liver cancers. In addition, the effect of dietary alterations on the growth of intrahepatically transplanted hepatomas will be evaluated.

Identifying number: R01 CA 23053
Principal investigator: Micheline M. Mathews-Roth
Institution: Peter Bent Brigham Hospital
Title: Carotenoids as Antitumor Agents for Skin Tumors

Total FY79 obligation: $40,341
Nutrition allotment: 100%
Nutrition funding: $40,341

Total FY80 obligation: $55,311
Nutrition allotment: 100%
Nutrition funding: $55,311

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

Carotenoid pigments will be used to attempt to inhibit the formation of tumors induced by ultraviolet light. Analysis of the numbers of tumors in hairless mice and the time of induction will indicate whether the systemic administration of carotenoids has any significant effect on tumor induction.

Identifying number: R01 CA 23156
Principal investigator: Richard N. Zare
Institution: Stanford University
Title: Laser Fluorescence Analysis

Total FY79 obligation: $66,611
Nutrition allotment: 100%
Nutrition funding: $66,611

Total FY80 obligation: $68,525
Nutrition allotment: 100%
Nutrition funding: $68,525

Laser Fluorescence Analysis (continued)

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Laser fluorimetry will be utilized to detect the presence of the mold metabolite, aflatoxin, and *N*-nitrosamines. It is anticipated that a reliable analytical procedure for detection will be produced that will lower present detection limits in contaminated food products by more than an order of magnitude.

Identifying number: R01 CA 23205
Principal investigator: Alfredo S. Lopez
Institution: Louisiana State University Medical Center
Title: Lung Cancer and Vitamin A

Total FY79 obligation: $92,598
Nutrition allotment: 100%
Nutrition funding: $92,598

Total FY80 obligation: $83,548
Nutrition allotment: 100%
Nutrition funding: $83,548

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This research is designed to ascertain the relationship between vitamin A and lung cancer. This study is being done in Louisiana, a state known to have very high incidence of lung cancer. Preliminary analysis of available data (National Nutrition Survey and HANES) indicates a negative correlation between beta-carotene (precursor of vitamin A) and mortality rates due to respiratory system cancers and also with mortality from all neoplasms, but not with total deaths.

Case-control studies have been initiated in which dietary intakes and vitamin A concentration in hepatic tissue of patients who died of lung cancer will be compared with appropriate controls. Studies have been started in living patients suffering from lung cancer. Serum concentrations and dietary intakes of vitamin A are measured and compared with those from matched controls. The information to be obtained from these studies would provide evidence for the suggested relationship between vitamin A and lung cancer.

Identifying number: R01 CA 23218
Principal investigator: Phillip Coffino/Henry R. Bourne
Institution: University of California, San Francisco
Title: Carcinogen Testing: A Mouse Lymphoma Mutation System

Total FY79 obligation: $59,583
Nutrition allotment: 10%
Nutrition funding: $5,958

Total FY80 obligation: $63,606
Nutrition allotment: 10%
Nutrition funding: $6,361

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Studies with both prokaryotic and eukaryotic cells suggest that the mutagenic activities of an organic compound can be used to test for and predict its carcinogenicity. Known carcinogens, aflatoxin B_1 (a food contaminant) and benzo[a]pyrene, will be used to test the sensitivity and efficacy of certain genetic markers.

Five hundred forty-nine Mouse lymphoma tissue culture cells will be used as the target for mutation induction. Five hundred forty-nine cells will be incubated with aflatoxin B_1 and benzo[a]pyrene and, after a suitable expression time, cloned in agar with each of the selective media to determine the frequency of induced mutation for each marker.

Identifying number: R01 CA 23449
Principal investigator: Benito Lombardi
Institution: University of Pittsburgh
Title: Choline Deficiency, Oval Cells, and Hepatocarcinogenesis

Total FY79 obligation: $80,141
Nutrition allotment: 100%
Nutrition funding: $80,141

Total FY80 obligation: $86,767
Nutrition allotment: 100%
Nutrition funding: $86,767

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Choline Deficiency, Oval Cells, and Hepatocarcinogenesis (continued)

Project description:

Feeding a choline-devoid diet to rats has been shown to have four distinct but related effects on the induction of hepatocellular carcinomas by chemical carcinogens: 1) a sensitization of the animals to low levels of chemical hepatocarcinogens; 2) a marked reduction in the latent period of hepatocellular carcinoma induction; 3) a high incidence of the tumors; and 4) a change, to liver, of the organ susceptibility of certain chemical carcinogens.

The long-term goal of this project is to elucidate the mechanism(s) whereby the dietary regimen modifies tumor induction so remarkably. Studies already performed indicate that a diet devoid of choline exerts a strong promoting action on the evolution of liver cells, initiated by a single exposure to a carcinogen, to foci of preneoplastic hepatocytes. At the same time, the diet appears not to affect the initiation stage of liver carcinogenesis.

Other studies performed, or in progress, are aimed at elucidating the nature, biochemical properties, and role in the process of hepatocarcinogenesis, of ductular cells and oval cells. Toward this goal, methodologies have been developed for the isolation, separation, and purification of ductular cells and of oval cells of rat liver.

Identifying number: R01 CA 23451
Principal investigator: Peter N. Magee
Institution: Temple University
Title: Formation and Metabolism of N-Nitroso Compounds

Total FY79 obligation: $133,739
Nutrition allotment: 10%
Nutrition funding: $13,374

Total FY80 obligation: $123,802
Nutrition allotment: 10%
Nutrition funding: $12,380

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The metabolism, including absorption, distribution in the body, interaction with cellular constituents, and excretion, of a number of selected N-nitroso compounds and their metabolic products will be studied in rats and other species. The N-nitroso compounds will include nitrosamines, nitrosamides, and nitrosamidines as well as methylhydrazines and phenyldimethyltriazene. Most of the compounds chosen are carcinogenic but some are reported to be noncarcinogenic. Emphasis will be placed on nitrosamides that are used in clinical human cancer chemotherapy, since these are the only N-nitroso compounds that are deliberately administered to human subjects. The compounds will be variously labeled with radioactive (^{14}C and ^{3}H) and stable (^{15}N and ^{13}C) isotopes. Nitrosamines will be measured in tissues and body fluids by a new method of differential pulse polarography that is currently being developed in these laboratories.

The metabolism of secondary amines that occur normally in the body, including dimethylamine, pyrrolidine, piperidine, proline, and sarcosine, will be studied in relation to their potential endogenous nitrosation under various conditions.

The metabolism of nitrate and nitrite will be studied, since relatively little is known in this area. Nitrite estimations in tissues and body fluids will be made by a new method based on nitrosation of diphenylamine. Nitrite and nitrate labeled with ^{15}N will be used in some of this work. The development and improvement of the new method for nitrosamine and nitrite determination will be a major part of the proposed research.

This research should increase knowledge concerning the role of alkylation reactions in carcinogenesis by nitroso compounds and the possible role that these compounds may play in the causation of animal and human cancer.

Identifying number: R01 CA 23514
Principal investigator: Edward Bresnick
Institution: University of Vermont and State Agriculture College
Title: DNA Repair After Polycyclic Hydrocarbon Administration

Total FY79 obligation: $87,145
Nutrition allotment: 40%
Nutrition funding: $34,858

Total FY80 obligation: $81,297
Nutrition allotment: 40%
Nutrition funding: $32,519

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This project will utilize the hamster model in which benzo[a]pyrene FE_2O_3 is instilled intratracheally to study DNA repair in the trachea. The goal is to determine the stability of benzo[a]pyrene (BP)-DNA adducts in traches, the aralkylation pattern of LH-20 Sephadex of the deoxyribonucleoside-polycyclic hydrocarbon complexes, and the DNA damage as assessed by an alkaline elution technique.

In addition, this study will determine the effects of vitamin A deficiency on the above parameters. It is known that this deficiency greatly increases the polycyclic hydrocarbon-induced incidence of squamous cell carcinomas in these hamsters.

Identifying number: R01 CA 23524
Principal investigator: Gerald Shklar
Institution: Harvard University
Title: Oral Carcinogenesis, Vitamin A, and Retinoids

Total FY79 obligation: $82,730
Nutrition allotment 100%
Nutrition funding: $82,730

Total FY80 obligation: $93,876
Nutrition allotment: 100%
Nutrition funding: $93,876

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

A series of investigations will be undertaken to determine whether vitamin A or synthetic retinoids administered systemically to experimental animals can delay or prevent chemical carcinogenesis of two oral mucosal DMBA model systems: hamster buccal pouch and hamster tongue.

Retardation of chemical carcinogenesis will be studied histologically, since these model systems are well defined in terms of the sequence of development of dysplasia, carcinoma in situ, and frank, invasive epidermoid carcinoma.

The distribution of retinoids in oral tissues will be studied by autoradiography. Possible mechanisms of the action of retinoids in retarding tumor development will be studied by immunologic assays for enhancement of cell-mediated immunity and by biochemical techniques for alterations related to cyclic AMP and the arachidonic acid-prostaglandin system.

Identifying number: R01 CA 23678
Principal investigator: Robert E. Click
Institution: University of Minnesota, Minneapolis
Title: Tolerance of Bone Marrow Grafts

Total FY79 obligation: $56,194
Nutrition allotment: 20%
Nutrition funding: $11,238

Total FY80 obligation: $52,011
Nutrition allotment: 20%
Nutrition funding: $10,402

Cancer activity/thrust: Immunology/Treatment Research

Project description:

For many patients, organ transplant remains the only form of treatment for their disease. However, immunological rejection of grafted organs, which may accompany marrow reconstitution, limits the potential of organ replacement as a therapeutic tool. The most direct means to establish organ replacement as a therapeutic tool is to define conditions by which tolerance to major as well as minor histocompatibility alloantigens could be achieved and maintained. Although a number of avenues to attain tolerance are being examined by various investigators, this project will concentrate on means of inducing tolerance to bone marrow cells such that the graft versus host (GVH) disease that usually results from reconstitution with marrow cells is avoided.

Generally the most successful reconstitution of animals (and patients) is achieved with bone marrow obtained from a donor that is identical to the recipient at the major histocompatibility locus: the H-2 complex of the mouse and the HLA complex of humans. In recent experiments the transfer of bone marrow cells from one strain of mouse into a lethally X-irradiated H-2 (K-end) disparite strain did not result in fatal GVH for over 300 days in 6 out of 10 animals injected, a finding which is opposite of what was expected. However, reconstitution of mice of a different strain, which had the same H-2 haplocyte as the first recipients, did result in death as expected in a rather short period after reconstitution.

The long-range goals of this research are to utilize the mouse system to 1) define the parameters, i.e., genetic or environmental, which determine the different mean survival times in the two H-2 identical strains of mice after reconstitution with H-2 disparite bone marrow cells; 2) determine the mechanism by which factors affect lymphocyte function; and 3) assess the usefulness of the mechanism underlying findings in mice for the reduction of tolerance to marrow grafts in humans.

Identifying number: R01 CA 23684
Principal investigator: Jarvis T. Chan
Institution: Texas Southern University
Title: Reversal of Cytotoxicity and Carcinogenesis by Antioxidants

Total FY79 obligation: $34,408
Nutrition allotment: 100%
Nutrition funding: $34,408

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Reversal of UV light-induced cytotoxicity by certain dietary antioxidants has been demonstrated in vitro. This system will now be used to study the prophylactic role of antioxidants in actinic carcinogenesis as well as the mechanism of UV light-induced skin carcinogenesis.

Identifying number: R01 CA 23714
Principal investigator: Stanley N. Gershoff
Institution: Tufts University
Title: Effect of Diet on Vesical Tumor and Stone Formation

Total FY79 obligation: $77,512
Nutrition allotment: 100%
Nutrition funding: $77,512

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objective of this research is to study the formation of urinary stones in experimental animals and the metabolic alterations responsible for their production. This will be done with the use of diets of varying vitamin and carbohydrate content with and without added oxalate precursors such as hydroxyproline and glycine.

A model will be developed for the rapid production of vesical cancer to enhance the study of morphological and metabolic changes associated with the development of this type of cancer. The projected work will encompass the relationships of diet, carcinogens, and initiation of the urinary bladder cancer by foreign bodies on the development of vesical tumors.

Identifying number: R01 CA 23901
Principal investigator: Stephen S. Hecht
Institution: American Health Foundation
Title: Metabolism and Carcinogenesis of Environmental Nitrosamines

Total FY79 obligation: $29,453
Nutrition allotment: 15%
Nutrition funding: $4,418

Total FY80 obligation: $65,561
Nutrition allotment: 15%
Nutrition funding: $9,834

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The metabolism and mechanism of action of the nitrosamines will be studied. Nitrosamines may be ingested preformed or formed in vivo through the reaction of nitrates or nitrites (food preservatives) with secondary amines present in common foods. Nitrosodiethanolamine occurs in the environment more than any other nitrosamine and nitrosopyrrolidene is also widely distributed; nitrosomorpholine is formed readily by nitrosation in vivo.

Metabolic profiles for these nitrosamines will be developed with special emphasis on the pathway of metabolic activation.

Identifying number: R01 CA 23927
Principal investigator: Thomas M. Mack
Institution: University of Southern California
Title: Case-Control Study of Malignant Melanoma

Total FY79 obligation: $123,615
Nutrition allotment: 2%
Nutrition funding: $2,472

Total FY80 obligation: $197,420
Nutrition allotment: 2%
Nutrition funding: $3,948

Case-Control Study of Malignant Melanoma (continued)

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

A case-control study will be made of cutaneous malignant melanoma. The objective of this study is to examine the association of malignant melanoma and a variety of putative antecedent risk factors including residential history, ethnicity, medical history, drug history, occupational history, life style, diet, family history, skin color, recreational and occupational exposure to solar radiation, hormonal factors, and habits of protection against the sun.

Cases will be identified over 4.5 years by the LAC/USC Cancer Surveillance Program, a large, population-based tumor registry providing identification of newly diagnosed cancer cases among the large and varied population of Los Angeles County. The population at risk includes over 5 million white residents with non-Spanish surnames. It is in a southern latitude and yields about 5 percent of the melanoma cases in the country. The primary source of case selection will be hospital pathology files. Hematology, cytology, and autopsy reports, surgical pathology records, and independent laboratory files are periodically searched for all microscopically diagnosed melanomas. Slides from each case will be requested and confirmed by independent pathology readings. Neighborhood residents of the same age, sex, and race will be used as controls. A detailed, pretested questionnaire will be administered by personal interview to each patient and control. Skin, hair, and eye color will be objectively classified.

Identifying number: R01 CA 23968
Principal investigator: Stephen Duck
Institution: Medical College of Wisconsin
Title: Therapy-Induced Growth Disorders in Childhood Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $70,561
Nutrition allotment: 100%
Nutrition funding: $70,561

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

Acute lymphocytic leukemia (ALL) is the most common malignancy of childhood. Currently about 50 percent of those children diagnosed as having ALL will survive for 5 or more years. With improved survival times, many serious adverse effects of cancer therapy are being manifested: some of these are leucoencephalopathy, disrupted growth and development, and neuroendocrine dysfunction. At present it is uncertain whether one can predict which children will experience these particular adverse effects and what if anything can be done to prevent expression of hormone dysfunction. The specific objectives are: 1) to establish if, at any stage of therapy for ALL, there is an impairment of the neuroendocrine-endocrine endorgan axis, and to what extent is such exposed clinically by disturbed growth and development; and 2) to establish what is the relative "necessity" and "potential benefit" of appropriately timed trials of exogenous hormone therapy based on the temporal characteristics of these endocrine disruptions. Methods will involve a 4-year prospective evaluation of newly diagnosed children with ALL. The new patients will be enrolled during the first 2 years of the study, allowing 2-3 year followup for the survivors. Each patient will be evaluated by extensive, sequential anthropometric parameters, bone age analyses, and basal and "stress"-released hormone levels, performed at each phase of cancer therapy.

Identifying number: R01 CA 24108
Principal investigator: Mary A. Hilton
Institution: University of Louisville
Title: Nutritional Intervention in Cancer Chemotherapy

Total FY79 obligation: $42,779
Nutrition allotment: 100%
Nutrition funding: $42,779

Total FY80 obligation: $42,387
Nutrition allotment: 100%
Nutrition funding: $42,387

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The protocol to be used will "rescue" lymphoma-bearing mice from lethal doses of the anticancer drug, methotrexate (MTX) with N-methyltetrahydrofolate ($N_5CH_3FH_4$) when the animals are maintained on a methionine-free diet containing DL-homocystine as the only sulfur amino acid. This regimen may provide selective "rescue" of normal cells in the presence of the L-1210 and L-5178Y neoplastic cells, which are known to be methionine dependent.

Studies on whole animals will be required to refine this protocol to compare tumor growth in treated and untreated animals. This work will include measurement in the tumor of the activities of enzymes involved in pathways in sulfur amino acid metabolism, i.e., methionine synthetase, methionine adenosyltransferase, S-adenosylhomocysteine hydrolase, cystathionine synthetase, cystathionase, and glycine N-methyltransferase.

Exploration of the molecular basis for the observed tumor growth in whole animal experiments will expand current understanding of the comparative biochemistry and sensitivity to MTX of these lymphoma cells. The knowledge obtained by the proposed research could lead to the use of nutritional manipulation as an adjuvant to established cancer chemotherapy programs.

Identifying number: R01 CA 24228
Principal investigator: Edwin A. Zepe
Institution: Kirksville College of Osteopathic Medicine
Title: Endocrine Factors in Cancer-Induced Lipolysis

Total FY79 obligation: $29,627
Nutrition allotment: 50%
Nutrition funding: $14,813

Total FY80 obligation: $30,827
Nutrition allotment: 50%
Nutrition funding: $15,414

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

Several reports have concerned the accelerated lipolysis primarily due to increased fatty acid mobilization that occurs in adipose tissue of experimental animals and humans with cancer. The objective of this project is to study the effects the Walker 256 experimental carcinoma might have on the circulating levels of various lipolytic and antilipolytic hormones, including norepinephrine, adrenocorticotopic hormone, and insulin.

Identifying number: R01 CA 24518
Principal investigator: Arthur M. Cohen
Institution: University of Southern California
Title: Inhibition of Carcinogenesis by Selenium

Total FY79 obligation: $67,607
Nutrition allotment: 100%
Nutrition funding: $67,607

Total FY80 obligation: $72,004
Nutrition allotment: 100%
Nutrition funding: $72,004

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This research will provide a better understanding of the molecular mechanisms underlying the protective effect of selenium against chemical carcinogenesis. Initial studies will be conducted to quantitate the effect of dietary selenium (0.5 ppm) on the incidence of hepatomas in rats fed 2-fluorenylacetamide. Subsequent experiments will focus on the possible relationship between the anticarcinogenic action of selenium and its function as a component of the enzyme, glutathione peroxidase (GPO). Specifically, an attempt will be made to correlate the activity of GPO in the livers of selenium-deficient and selenium-supplemented rats with hepatic malondialdehyde concentrations at various intervals after the addition of FAA to their diets.

Other studies will be concerned with the effect of selenium on the metabolism of FAA both in vivo and in vitro. Recently developed high-pressure liquid chromatography techniques will be used to separate and quantitate metabolites of FAA excreted in the urine. By similar means the effect of dietary selenium on the metabolism of FAA by hepatic microsomes in vitro will be quantitated.

Finally, the effect of selenium on the binding of FAA to hepatic DNA will be investigated. The effect of selenium on the amount of carcinogen initially bound to DNA as well as its effect on the retention of DNA-bound FAA at later intervals will be studied. In conjunction with the studies described above, these investigations should provide new insights into the ability of selenium to protect the liver against potential changes in gene function induced by FAA.

Identifying number: R01 CA 24549
Principal investigator: Diane F. Birt
Institution: University of Nebraska Medical Center
Title: Influence of Dietary Selenium on Pancreatic Cancer

Total FY79 obligation $85,777
Nutrition allotment: 100%
Nutrition funding: $85,777

Total FY80 obligation: $183,945
Nutrition allotment: 100%
Nutrition funding: $183,945

Influence of Dietary Selenium on Pancreatic Cancer (continued)

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

A relationship has been established between selenium intake and cancer at numerous sites in experimental animals, and an association has been suggested between selenium intake and pancreatic cancer in humans. Development of an appropriate pancreatic cancer model in the Syrian golden hamster has made it possible to evaluate the possible influence of dietary selenium on experimental pancreatic cancer.

Short-term and chronic studies are planned which will evaluate the relationship. In the short-term study, the selenium requirement and the effects of selenium deprivation and excess will be determined in the Syrian hamster. Data from this study will be utilized to establish selenium levels to feed in a life-span study on pancreatic carcinogenesis. The effects of the type of dietary selenium will be evaluated by feeding sodium selenite and seleno DL-methionine. The influence of excess and restriction will be observed, and the effects of feeding these amounts before and after treatment with the carcinogen will be determined.

In addition, these studies will evaluate the effects of life-span feeding of three levels of selenium (a proposed anticarcinogen) on longevity and general health in the Syrian golden hamster.

Identifying number: R01 CA 24616
Principal investigator: Paul I. Musey
Institution: Emory University
Title: Diet Effect on Estrogen Biosynthesis and Metabolism

Total FY79 obligation: $68,974
Nutrition allotment: 100%
Nutrition funding: $68,974

Total FY80 obligation: $73,783
Nutrition allotment: 100%
Nutrition funding: $73,783

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Intestinal microflora may have an active role in the biosynthesis and metabolism of estrogens. The intestinal microflora could form these estrogens through metabolism of estrogen conjugates secreted into or present in the intestinal lumen. Alterations in diet may produce significant changes in the intestinal microflora that result in altered biosynthesis and estrogens in the blood and urine.

Two possible mechanisms for the difference in the formation of estrogens in the various groups are 1) a difference in the intestinal microflora capable of biosynthesis and/or metabolism of estrogens, and 2) increased amounts of sterols, neutral steroids, or bile acids in the intestinal lumen for conversion to estrogens by the intestinal microflora. Either of these mechanisms would lead to an alteration in the intraluminal pattern of estrogens available for reabsorption.

Standard in vivo and in vitro techniques will be used to demonstrate a difference in the intraluminal pattern of estrogen after significant alteration of the diet and that this difference is reflected in vivo by altered blood and urine levels. If these relationships can be shown to exist, they may explain why the pattern of estrogens is different in individuals at high risk to breast cancer. Furthermore, an important environmental factor (diet) may be identified in the induction of breast carcinoma.

Identifying number: R01 CA 24856
Principal investigator: Arlan G. Richardson
Institution: Illinois State University
Title: Age-Related Changes in Chemical Carcinogenesis

Total FY79 obligation: $48,921
Nutrition allotment: 100%
Nutrition funding: $48,921

Total FY80 obligation: $47,600
Nutrition allotment: 100%
Nutrition funding: $47,600

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Aflatoxins, natural food toxicants produced by the common mold Aspergillus flavus, may contaminate foodstuffs such as cassava, beans, peas, peanuts, cereals, and groundnuts.

The objective of this study is to determine whether biochemical change in the cellular metabolism of aflatoxin by the liver occurs in an organism as it ages and, if so, whether these changes can be correlated with an increased vulnerability to cancer. Special attention will be given throughout the study to the effect of age on the formation of aflatoxin-DNA adducts in rats 4 to 30 months of age.

Identifying number: R01 CA 24959
Principal investigator: Samuel S. Epstein
Institution: University of Illinois Medical Center
Title: Quantitative Carcinogenesis Projection Between Species

Total FY79 obligation: $39,250
Nutrition allotment: 10%
Nutrition funding: $3,925

Total FY80 obligation: $43,165
Nutrition allotment: 10%
Nutrition funding: $4,317

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The aim of this project is to investigate the feasibility of quantitative extrapolation of carcinogenesis data from species to species. Among the carcinogens to be fit into carcinogenesis models are aflatoxin B_1, saccharin, and dimethylnitrosamine. The models will make predictions of both dose-response relations and time-to-tumor relations.

Identifying number: R01 CA 25002
Principal investigator: Richard A. Scanlan
Institution: Oregon State University
Title: N-Nitrosamines in Foods

Total FY79 obligation: $92,804
Nutrition allotment: 100%
Nutrition funding: $92,804

Total FY80 obligation: $99,626
Nutrition allotment: 100%
Nutrition funding: $99,626

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This project is to investigate the occurrence and formation of N-nitrosamines in food and to evaluate the hazard of the compounds formed. The thermal energy analyzer will be used to measure nitrosamines in actual food samples. Tests will be run on a variety of seafood products suspected to contain N-nitrosamines, such as fishmeal.

Identifying number: R01 CA 25012
Principal investigator: Peter R. Sinclair
Institution: Dartmouth College
Title: Liver Cell Culture for Study of Carcinogen Activation

Total FY79 obligation: N/A

Total FY80 obligation: Active, not funded
Nutrition allotment: 5%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The ultimate goal of this project is the development of liver cells in tissue culture suitable for studies of in vitro chemical carcinogenesis. Available liver cell cultures and liver cell lines retain only a small fraction of mixed function oxidase (MFO) activities of the intact liver. It is these activities which involve cytochrome P-450 as the oxidase that activate carcinogens. We propose to determine whether the decrease in MFO activities is due to decreased synthesis or increased turnover of heme, the prosthetic group of cytochrome P-450. In addition, the reason for the decreased responsiveness of the cultured cells to chemicals which induce increases of MFO activities in the intact rat will be investigated. Primary cultures of embryonic chick and adult rat will be used as model systems for study of these phenomena because of the investigators' experience with them. The chick embryo system seems particularly promising because of its known in vivo-like responsiveness to chemical inducers of delta-aminolevulinate synthetase, the rate-limiting step for heme biosynthesis. Sensitive fluorometric and radioactive assays will be used for heme synthesis and MFO activities. Attempts will be made to change the culture conditions in order to correct the lesion(s) that resulted in decreased MFO activities. Once optimal conditions are established for maintenance and, if possible, inducibility of MFO activities, the abilities of cells to produce activated carcinogens will be assessed by the Ames assay for mutagens of Salmonella and the binding of radioactive carcinogen metabolites to cellular macromolecules.

Identifying number: R01 CA 25073
Principal investigator: Graham R. Underwood
Institution: New York University
Title: Study of Ultimate Carcinogen from Aromatic Amines

Total FY79 obligation: N/A

Study of Ultimate Carcinogen from Aromatic Amines (continued)

Total FY80 obligation: $52,578
Nutrition allotment: 20%
Nutrition funding: $10,516

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Studies of the fundamental chemical behavior of nitrenium ions, which are the ultimate carcinogens derived from aromatic amines, will be undertaken These will involve: 1) molecular orbital calculations on model systems and nitrenium ions; 2) metagenic assays on modified molecules similar to the nonmutagenic 1-naphthylamine; 3) 0-18 labeling of the o-acetylarylhydroxamic acid derived from the carcinogenic and noncarcinogenic amines in order to study the involvement of ion pairs in the carcinogenic reaction; and 4) study of the rates and products of reaction of the nitrenium ion precursors with various nucleophiles.

Identifying number: R01 CA 25089
Principal investigator: Edward M. Kaighn
Institution: Pasadena Foundation for Medical Research
Title: Culture and Carcinogenesis of Human Bladder Urothelium

Total FY79 obligation: $72,669
Nutrition allotment: 20%
Nutrition funding: $14,534

Total FY80 obligation: $59,025
Nutrition allotment: 20%
Nutrition funding: $11,805

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The main objective of this project is to investigate the role of promoters, inhibitors, and nutritional factors in bladder carcinogenesis. For development of a model culture, normal human bladder epithelial cell lines and direct bladder carcinogens will be employed. The system will make it possible to study the action of chemical carcinogens in the appropriate target cell.

Identifying number: R01 CA 25094
Principal investigator: Emmanuel Farber
Institution: University of Toronto
Title: Short-Term In Vivo Assay for Carcinogens

Total FY79 obligation: \$57,614
Nutrition allotment: 5%
Nutrition funding: \$2,881

Total FY80 obligation: \$60,891
Nutrition allotment: 5%
Nutrition funding: \$3,045

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The objective of this research is the development of a short-term in vivo assay for carcinogens generally, with the use of intact liver as the activator as well as the indicator and an early step in cancer development as the biological endpoint.

Identifying number: R01 CA 25167
Principal investigator: Roger M. Herriot
Institution: Johns Hopkins University
Title: Pyrolytic Products of Proteinous Foods as Mutagens

Total FY79 obligation: \$44,319
Nutrition allotment: 100%
Nutrition funding: \$44,319

Total FY80 obligation: \$50,985
Nutrition allotment: 100%
Nutrition funding: \$50,985

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Several Japanese laboratories have found that substances in broiled fish and meat and in pyrolyzed proteins or certain amino acids are Ames test positive mutagens when activated by rat liver microsomes. In view of the correlation between mutagens and carcinogens, it is implied but not demonstrated that these mutagens are probably carcinogens.

It is planned to prepare the pyrolytic product of 1-tryptophan, $TrpP_2$, which, on activation, is a powerful mutagen. Its mutagenic action on transforming DNA and its carcinogenic action in rats will be

Pyrolytic Products of Proteinous Foods as Mutagens (continued)

determined. Use of naked transforming DNA, free in solution in place of Ames test bacteria, permits a better evaluation of structure of the activated mutagen and of the process of mutagenesis.

An analysis of the activation reaction and identification of the activated form are planned as well as a study of the bases in DNA with which the activated mutagen reacts. The public health implications of the pyrolysis products are emphasized as well as the need for a thorough study of the problem.

Identifying number: R01 CA 25264
Principal investigator: Ralph S. Paffenbarger, Jr.
Institution: Stanford Universty
Title: Early Predictors of Site-Specific Cancers

Total FY79 obligation: $107,050
Nutrition allotment: 5%
Nutrition funding: $5,353

Total FY80 obligation: $113,169
Nutrition allotment: 5%
Nutrition funding: $5,658

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This study has two objectives: 1) to extend observations on approximately 51,500 students at the University of Pennsylvania in order to identify characteristics of college and alumni years predictive of site-specific and total cancer later in life, and 2) to develop improved methods for detecting combinations of their protective characteristics. Among the factors to be examined are lifestyle patterns, including diet.

Identifying number: R01 CA 25362
Principal investigator: Hira I. Gurtoo
Institution: Roswell Park Memorial Institute
Title: Genetics of Aflatoxin Metabolism: Role in Carcinogenesis

Total FY79 obligation: $19,982
Nutrition allotment: 100%
Nutrition funding: $19,982

Total FY80 obligation: $37,167
Nutrition allotment: 100%
Nutrition funding: $37,167

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This research involves investigations of the genetic regulation of aflatoxin B_1 metabolism via activation and deactivation paths of environmental factors, i.e., polycyclic aromatic hydrocarbons (PAH's) that determine the genetic regulation of AFB_1 metabolism in mice, the metabolism of AFB_1 in humans, and the role of the genetics of AFB_1 metabolism in carcinogenesis and toxicity. Compounds to be studied will include AFB_1 and substances that cause induction or repression of the specific pathways of AFB_1 metabolism.

The objectives of these studies are 1) to understand the genetic regulation of AFB_1 metabolism via various pathways, including activation and detoxification; 2) to develop genetic models for studies on aflatoxin carcinogenesis and toxicity; 3) to define the role of the genetic regulation of AFB_1 metabolism via various pathways in the determination of susceptibility to aflatoxin B_1; and 4) to study the effect of smoking on the metabolism of AFB_1 by placental tissue obtained post delivery.

Much of the work will be performed 1) in vitro with labeled AFB_1, DNA, hepatic microsomes and other subcellular fractions isolated from rats, and human placental tissue, and 2) in vivo with different strains of rats and mice for the purpose of investigating the correlation between in vitro metabolism and in vivo metabolic activation in an effort to assess the role of the genetics of AFB_1 metabolism in toxicity and carcinogenesis.

Particular methods to be used include radiochemical techniques, thin-layer chromatography, spectroscopy, ultracentrifugation techniques, HPLC, and other biochemical and enzymological methods.

Identifying number: R01 CA 25382
Principal investigator: Paul M. Newberne
Institution: Massachusetts Institute of Technology
Title: Zinc, Nitrosamine, and Esophageal Cancer

Total FY79 obligation: $88,332
Nutrition allotment: 100%
Nutrition funding: $88,332

Zinc, Nitrosamine, and Esophageal Cancer (continued)

Total FY80 obligation: $94,781
Nutrition allotment: 100%
Nutrition funding: $94,781

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This study will determine the effects of a deficiency and excess of zinc on development of esophageal tumors in rats given methylbenzyl nitrosamine. Since alcohol consumption is associated with cancer of the esophagus in U.S. males, this factor will also be examined.

Preliminary studies have shown a derangement in tissue concentration of zinc and other trace elements and a significantly shorter lag period in tumor development, which suggest a potential risk in marginal zinc deficiency. An excess of zinc will be given rats to determine effects on tumor inhibition. Two zinc-dependent enzymes will be determined. Tissue distribution of labeled nitrosamine will be evaluated in deficient and control animals.

Identifying number: R01 CA 25484
Principal investigator: John S. Bertram
Institution: Roswell Park Memorial Institute
Title: Inhibition of In Vitro Transformation by Retinoids

Total FY79 obligation: $59,007
Nutrition allotment: 80%
Nutrition funding: $47,205

Total FY80 obligation: $68,239
Nutrition allotment: 80%
Nutrition funding: $54,591

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The retinoids, a group of natural and synthetic analogs of vitamin A, have been shown to possess anticarcinogenic properties in vivo. Natural retinoids will completely eliminate the expression of carcinogen-induced morphological transformation in cultured C3H/10T1/2CL8 cells. This project is to study the mechanism whereby retinoids can inhibit transformation.

The effects of retinoids on transformation will be examined in detail, and attempts will be made to isolate initiated cells. The relationship between tumor promoters and retinoids will also be investigated, and the effects of the retinoid content of feral serum will be studied. It is planned to investigate the biochemical aspects of retinoid activity. With the use of parental C3H/10T1/2 cells, initiated cells, and transformed cells, the effects of retinoids will be studied on 1) the biosynthesis of membrane glycolipids and glycoproteins with the use of labeled membrane precursors, and 2) the behavior of cell membranes with the use of the fluorescence recovery after photobleaching technique to measure membrane mobility and by a modification of the technique membrane fluidity. Levels of retinoic acid-binding protein and of retinol-binding protein will be measured in the cytosol of parental, initiated, and transformed cell lines.

Identifying number: R01 CA 25538
Principal investigator: Adrianne E. Rogers
Institution: Massachusetts Institute of Technology
Title: Dietary Fat, Prolactin, and Mammary Cancer

Total FY79 obligation: $123,497
Nutrition allotment: 100%
Nutrition funding: $123,497

Total FY80 obligation: $124,938
Nutrition allotment: 100%
Nutrition funding: $124,938

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This study will demonstrate the effects of long-term ingestion of high-fat diets on serum prolactin and on induced and spontaneous mammary tumors in rats. The relationship between fatty acid composition and hormonal and tumorigenic effects will be defined. Evidence that ingestion of a high-fat diet enhances rat mammary tumorigenesis will be assessed with the use of DMBA-induced tumor incidence in rats fed one of several dietary fats. Natural dietary fats of widely varying fatty acid composition will be fed as a purified diet, serum prolactin will be monitored by RIA, and DMBA-induced and spontaneous mammary neoplasms will be identified. The possibility of predicting ultimate tumor response of the individual from serum prolactin profiles will be determined by comparison of periodic serum prolactin paired values (proestrus: metestrusdiestrouso with tumor development). The distribution of prolactin receptors in various mammary lesions will be determined by

Dietary Fat, Prolactin, and Mammary Cancer (continued)

autoradiographic procedures. Dietary fat effects on the pathogenesis and incidence of spontaneous or induced benign or malignant mammary tumors will be differentiated.

Identifying number: R01 CA 25560
Principal investigator: Carter E. Carlton, Jr.
Institution: Baylor College of Medicine
Title: Bladder Cancer Chemistry: Tryptophan Metabolism

Total FY79 obligation: N/A

Total FY80 obligation: $41,259
Nutrition allotment: 100%
Nutrition funding: $41,259

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

The objective of this research proposal is to study the recurrence rate of bladder tumors in patients following correction of abnormal tryptophan metabolism. This investigation will concentrate on those tumor patients showing an abnormal urinary excretion pattern of tryptophan metabolites following an oral tryptophan load. Clinical trials will evaluate the effect of pyridoxine (vitamin B_6) on recurrence rate of bladder tumors.

The methods employed will be: 1) selection of patients with grade O or A tumors; 2) analysis of 24-hour urinary tryptophan metabolites before and after the ingestion of L-tryptophan; and 3) clinical trials utilizing pyridoxine and placebo in a double-blind study.

The purpose of the research is to elucidate the long-term recurrence rate of heterotopic bladder tumors in those patients whose abnormal tryptophan metabolism has been corrected.

Identifying number: R01 CA 25580
Principal investigator: Ann W. Sorenson/Dee W. West
Institution: University of Utah
Title: Diet and Colon Cancer in Humans: The Effects of Fiber

Total FY79 obligation: $467,285
Nutrition allotment: 100%
Nutrition funding: $467,285

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This case-control study will attempt to find relationships between dietary fiber and colon cancer etiology. The dietary fiber intake of Utah residents, a low-risk population for colon cancer, is believed to be higher than other U.S. populations because of the high consumption of home-preserved foods, i.e., fruits, vegetables, and cereal grains.

Identifying number: R01 CA 25602
Principal investigator: Guglielmo De Rosa
Institution: University of Louisville
Title: Dietary Modifications, Exercise, and Tumor Growth

Total FY79 obligation: $79,800
Nutrition allotment: 100%
Nutrition funding: $79,800

Total FY80 obligation: $82,842
Nutrition allotment: 100%
Nutrition funding: $82,842

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Some of the metabolic parameters that might contribute to the high incidence of tumors observed in old age will be studied in experimental animals. The modifications of these parameters after long-term dietary restrictions or physical training will also be identified. The purpose of this study is to determine the correlation between the age-related changes in 1) body weight and composition, 2) efficiency of energy utilization, and 3) maintenance requirements and tumor development.

The influence of dietary manipulation and physical exercise on these age-related changes will be studied in order to evaluate 1) the mechanism by which long-term dietary restriction decreases tumor incidence, and 2) the possibility of obtaining the same effects by physical exercise. Rats of the following age groups will be considered: 21, 60, 100, 300, and 600 days.

The efficiency of energy utilization for growth will be determined by daily feeding four groups of rats a semipurified 24 percent casein diet for 21 days at four different levels of energy intake. On the 21st day the animals will be killed; changes in body weight will be correlated with the metabolizable energy intake (MEI) per metabolic body size (MBS); the slope of the regression line will indicate the efficiency of energy utilization for body growth. Body composition will be analyzed by freeze-drying and solvent extraction of the carcasses. Changes in lean and fat mass will be correlated with MEI/MBS, the slope of the lines obtained by regression analysis will indicate the coefficients of energy utilization for lean and adipose mass deposition. The x-axis intercepts of the regression lines will indicate the MEI/MBS for maintenance of each body compartment. The rates of tumor growth will be determined by inoculating a cell suspension of a 7800 Morris hepatoma in the hind legs of some animals, harvesting and weighing the tumor after 21 days. Efficiency of energy utilization, maintenance requirements, and body composition of tumor-bearing animals will be measured. Dietary restriction will be obtained by feeding each age group restricted amounts of a 24 percent casein diet for 30 days. The influence of physical exercise will be studied by training the animals of each age group in motorized cages for 30 days.

Identifying number: R01 CA 25679
Principal investigator: Nurul H. Sarkar
Institution: Sloan-Kettering Institute for Cancer Research
Title: Effect of Diet on Murine Mammary Tumorigenesis

Total FY79 obligation: N/A

Total FY80 obligation: $120,692
Nutrition allotment: 100%
Nutrition funding: $120,692

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Total calorie restricted diets dramatically decrease the incidence of spontaneous tumors in strains of mice with a high incidence of murine mammary tumor virus (MuMTV) induced mammary cancer. Since the development of mammary tumors in mice results from an interplay of MuMTV, hormones and the immune system, we propose to study the effect of restricted calorie intake on each of these factors in various mouse strains. In these studies we will use C3H, GR, GRf and RIII mice which have a high incidence of naturally occurring mammary tumors. Mice from strains with a low incidence of mammary tumors (C57BL, BALB/c) will also be used and will be exogenously infected with MuMTV or given agents which normally enhance tumorigenesis, such as hormones or chemical carcinogens. The effect of calorie restriction on the mammary tumor incidence in all strains of mice will be determined and expression of MuMTV in these mice will be monitored by electron-microscopic, immunological and biochemical techniques. We will also determine if hormone receptors or the levels of circulating hormones that are important to mammary gland and tumor development are altered as a result of dietary restriction. Since calorie restriction may prevent the progression of preneoplastic nodules (HAN's) in mice to malignant tumors, we will transplant HAN's into MuMTV-producing or nonproducing syngeneic mice fed normal or restricted diets in order to determine if hormones and/or viral expression affect the progression of HAN's to tumors. In vitro organ culture of mammary glands in the presence of hormones and/or virus prior to transplantation will be used to determine how these factors affect the transformation of HAN's into tumors. We will also examine the way in which diet affects the humoral and cellular immune response of both high and low tumor incidence strains of mice. As a result of these investigations, we hope to understand the mechanims by which the interaction between MuMTV, hormones, and the immune response may be altered by diet in such a way as to affect murine mammary tumorigenesis.

Identifying number: R01 CA 25693
Principal investigator: Raymond L. Blakley
Institution: University of Iowa
Title: Methotrexate Toxicity and Rescue

Total FY79 obligation: N/A

Total FY80 obligation: $66,887
Nutrition allotment: 25%
Nutrition funding: $16,721

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Methotrexate Toxicity and Rescue (continued)

Project description:

Human lymphoblastoid cells in culture will be used to determine uptake, influx and efflux of methotrexate under various conditions and the effect on it of 5-formyltetrahydrofolate (leucovorin) and 5-methyltetrahydrofolate. Transport of these reduced folates and the effect on it of methotrexate will also be studied. Metabolism of methotrexate to polyglutamate derivatives under various conditions and metabolism of the one-carbon and pteridine moieties of leucovorin and methyltetrahydrofolate under various conditions will be studied. The effect of methotrexate at various intracellular concentrations on various biosynthetic processes will be studied as well as the ability of various combinations of agents to rescue cells after exposure to methotrexate for various lengths of time and various external concentrations of methotrexate.

Identifying number: R01 CA 25786
Principal investigator: Josef E. Fischer
Institution: University of Cincinnati
Title: A Central Mechanism for Anorexia in Cancer

Total FY79 obligation: $79,492
Nutrition allotment: 100%
Nutrition funding: $79,492

Total FY80 obligation: $98,264
Nutrition allotment: 100%
Nutrition funding: $98,264

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

Recent studies have focused on the potential value of nutritional support to the patient with neoplastic disease. Concomitantly, interest has increased in the anorexia/cachexia syndrome in patients with cancer, a syndrome in which patients, with, at times, early tumors, manifest weight loss secondary to reduced intake out of proportion to their tumor burden. One of the theories of the etiology of this syndrome is that certain metabolic changes brought about by the tumor affect the central "appetite-satiety center" in such patients. Recent neurophysiological studies have focused attention on the appetite-satiety center, so called, as perhaps involving indoleamine (serotonin) and catecholamine (norepinephrine, dopamine neurotransmitters). The planned studies are related to the hypothesis, supported by preliminary experiments, that in animals with implanted Walker-256 carcinosarcoma tumors, anorexia, in an early manifestation, is causally related to increased synthesis of brain serotonin.

Studies address the nature of alterations in the metabolism of tryptophan, tyrosine, and phenylalanine, precursors of these neurotransmitters, and factors controlling their penetration of the blood-brain barrier, including plasma-free and total tryptophan, nonesterified fatty acids, plasma neutral amino acid ratios, and serum albumin. If these hypotheses prove correct, manipulation of the plasma concentrations of free or total tryptophan or other members of the competing large neutral amino acid group or the administration of central serotonin antagonists may prevent the development of anorexia. Similar studies measuring plasma-free and total tryptophan as well as plasma amino acid patterns will be done in patients with anorexia in the presence of neoplastic disease and after therapy when anorexia is no longer present.

Identifying number: R01 CA 25794
Principal investigator: Adelbert E. Wade
Institution: University of Georgia
Title: Effect of Dietary Fat Type on Chemical Carcinogenesis

Total FY79 obligation: $38,299
Nutrition allotment: 100%
Nutrition funding: $38,299

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

That dietary fats alter susceptibility to chemically induced cancer has been demonstrated through epidemiological studies of human populations and studies of laboratory animals.

The mechanism by which responses to chemical carcinogens are altered is unknown. However, reasonable assumptions are that diet induces changes which increase or decrease tissue reactivity to carcinogen, or that diet influences activity of the mixed-function oxidases which are responsible for the metabolic activation or detoxification of carcinogen.

The objectives of this research are to determine the influences of type of dietary fat on the activity of the mixed-function oxidases of rat liver as these oxidases participate in the metabolic activation and/or

Effect of Dietary Fat Type on Chemical Carcinogenesis (continued)

detoxification of the potential carcinogens 3,4 benzo[a]pyrene, 2-acetylaminofluorene, and dimethylnitrosamine. With the use of hepatic microsomes from control and carcinogen-pretreated rats fed the specified saturated or unsaturated fats for 1 to 6 weeks, the in vitro metabolism of each carcinogen will be assessed.

The apparent kinetics for the formation of each metabolite will be individually calculated. Correlation of metabolite and kinetic data with alterations in mutagenicity to appropriate strains of Salmonella with the use of the reverse mutation system of Ames will indicate the significance of changes induced by dietary fats in chemical carcinogenesis.

Correlation of metabolite and kinetic data with concentration and activity of components of the mixed-function oxidase system will identify underlying physiologic processes altered by dietary fats.

Identifying number: R01 CA 25970
Principal investigator: Nicholas J. Lowe
Institution: University of California, Los Angeles
Title: UV Light and Epideronal Polyamine and DNA Synthesis

Total FY79 obligation: $77,057
Nutrition allotment: 10%
Nutrition funding: $7,706

Total FY80 obligation: Active not funded
Nutrition allotment: 10%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The molecular basis for ultraviolet light carcinogenesis is a matter of speculation. Recently, the principal investigator has found that UVL produces dramatic increases in epidermal ornithine decarboxylase (ODC).

ODC, which forms putrescine by decarboxylation of ornithine, is the first and probably the rate limiting enzyme in the biosynthesis of the polyamines, spermidine and spermine. The activities of ODC and the levels of its biosynthetic products are elevated in various systems stimulated to proliferate. Furthermore, numerous studies indicate that the polyamine biosynthetic enzymes are implicated in neoplastic growth. For example, application of a potent tumor promoting agent, 12-Otetradecanoyl-phorbol-12-acetate (TPA) to mouse skin led to more than 250-fold increases in epidermal ODC activity and this phenotypic change is thought to be essential for skin tumor promotion.

In view of the potential significance of ODC for growth carcinogenesis, it is proposed to study in greater detail the response of epidermal ODC to UVL.

The effects of various drugs which may modify this UVL-induced epidermal ODC activity will be examined.

It may be possible to use inhibition of UVL-induced ODC epidermal activity as a means for screening agents that are protective against UV carcinogenesis. Can studies of UVL-induced epidermal ODC help to determine which are the least carcinogenic UV light sources for treatment of certain skin diseases, including psoriasis?

Identifying number: R01 CA 26030
Principal investigator: Rajendra G. Mehta
Institution: IIT Research Institute
Title: Retinoids and Mammary Carcinogenesis

Total FY79 obligation: $62,829
Nutrition allotment: 100%
Nutrition funding: $62,829

Total FY80 obligation: $66,687
Nutrition allotment: 100%
Nutrition funding: $66,687

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Morphological and biochemical procedures will be used to determine the effects of retinoids on the structural and functional differentiation of the mammary gland both in vivo and in vitro.

In addition, retinoid effects on the development of carcinogen-induced hyperplastic alveolar nodule-like structures in vitro and their potential to develop tumors upon subsequent transplantation will also be studied.

Extensive characterization of retinoic acid-binding protein in normal and neoplastic mammary tissues will also be made and retinoid receptor levels will be correlated with estradiol receptors in respective tissues. Investigations will be made to determine the effects of retinoids on serum prolactin levels.

Retinoids and Mammary Carcinogenesis (continued)

Finally, the validity of the evident mechanism(s) by which retinoids act will be examined in vivo.

Identifying number: R01 CA 26063
Principal investigator: William H. Douglas
Institution: Tufts University
Title: Primary Culture of Prostatic Epithelial Cells

Total FY79 obligation: N/A

Total FY80 obligation: $82,778
Nutrition allotment: 15%
Nutrition funding: $12,416

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

We plan to investigate parameters that will affect the differentiated structure and function of the primary epithelial cell cultures from both the dog and rat. These include: supplementation of the culture medium with hormones (including sex hormones) and growth factors; growing the cells on various substrates including prostate derived fibroblasts, fibronectin, and collagen matrices. The effects of these perturbations on androgen metabolism, acid phosphatase production, ornithine decarboxylase production, steroid binding capacity and formation of secretory granules and intercellular junctions will be monitored.

Identifying number: R01 CA 26135
Principal investigator: Eric Eisenstadt
Institution: Harvard University
Title: Mutagenic Specificity of Environmental Carcinogens

Total FY79 obligation: $111,199
Nutrition allotment: 25%
Nutrition funding: $27,800

Total FY80 obligation: $110,935
Nutrition allotment: 25%
Nutrition funding: $27,734

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The basic objective of this research program is to develop specific information about the spectrum of mutations that can be induced by environmental carcinogens, including food and water contaminants. This will be a study, at the nucleotide level, of the DNA alterations generated by carcinogens. Determination will be made of the mutagenic spectrum induced by benzo[a]pyrene 2-acetylaminofluorene, aflatoxin B_1, and ultraviolet light in bacteria with different DNA repair capabilities.

Identifying number: R01 CA 26156
Principal investigator: Steven R. Tannenbaum
Institution: Massachusetts Institute of Technology
Title: Carcinogenic Nitrosamines From Primary Amines

Total FY79 obligation: $77,174
Nutrition allotment: 50%
Nutrition funding: $38,587

Total FY80 obligation: $81,181
Nutrition allotment: 50%
Nutrition funding: $40,591

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

It has been hypothesized that some carcinogenic N-nitroso compounds found in the gastrointestinal tract are the result of the reaction between ingested nitrates and secondary amines produced by intestinal flora or ingested in foods such as cereals, tea, and meat, in bread-flavoring agents, in some commercially canned foods cooked in steam, or in tobacco smoke. The objective of this research is to determine whether in vivo nitrosation of primary amines in the gastrointestinal tract might also contribute to human exposure to these compounds.

Identifying number: R01 CA 26164
Principal investigator: George S. Smith
Institution: University of California Los Angeles
Title: Dietary Restriction, Cancer, and Immune Functions

Total FY79 obligation: $47,651
Nutrition allotment: 100%
Nutrition funding: $47,651

Dietary Restriction, Cancer, and Immune Functions (continued)

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Assessment will be made of the influence of gradually imposed, adult-initiated controlled dietary restriction on spontaneous carcinogenesis in A.CA/Sn male mice, an H-2 cogenic strain which develops pulmonary tumors and hepatomas. The effect of age at time of initiation of underfeeding will be tested as individually caged mice consuming since weaning a semisynthetic diet in amounts allowing "normal" growth will be dietarily restricted at either 5 months or 10 months of age. The diets used will supply the same per week amounts of protein (casein), vitamins, and salts to all mice, but calories will be limited for restricted mice such that they consume 70 percent the per week amount as do controls during the first month of underfeeding and 55 percent thereafter.

These diets produce undernutrition, not malnutrition. Dietary influences on the aging immune apparatus will be measured with emphasis on immunologic suppressor effects. Mice will be killed for evaluation of several age-sensitive immune indices at 14-15 and 19-20 months of age. These include lymphocyte proliferation (alloantigen or mitogen-stimulated tritiated thymidine uptake in vitro; colony growth in soft agar), humoral immune response (plaque-forming cell levels to sheep erythrocytes after in vitro sensitization) and lymphocytoxicity (cytolytic response to an allogeneic tumor after in vitro sensitization).

Manipulation of these basic assays will reveal the level of suppressor activity that seems to increase in tumor-bearing hosts and with advancing age. Effects of tumor type on these immunologic parameters will also be determined. This study should further define the efficacy of adult-onset dietary restriction as an inhibitor of spontaneous carcinogenesis that was observed in much earlier studies and not further explored. This phenomenon will be reevaluated with the use of improved diets and feeding strategies with an emphasis on the role of immunologic phenomena.

Identifying number: R01 CA 26355
Principal investigator: Michael L. Murray
Institution: Louisiana State University Medical Center
Title: Mediation of Nitrous Acid Mutagenesis by Polyamines

Total FY79 obligation: $44,034
Nutrition allotment: 50%
Nutrition funding: $22,017

Total FY80 obligation: $37,757
Nutrition allotment: 50%
Nutrition funding: $18,879

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Polyamines, abundant and ubiquitous components of the diet, are highly mutagenic when reacted with nitrite, a food additive and also a normal component of the diet.

The possibility that the mutagenic action of nitrous acid is a consequence of reaction with endogenous amines will be investigated by extraction of the prospective mutagens from cells which have been treated with nitrous acid.

Nitrate-polyamine reaction products will be 1) tested for their action on prokaryotic and eukaryotic cells with defects related to repair and/or replication; 2) tested for their action on specific enzymatic reactions related to repair and/or replication; 3) examined for in vivo alkylation reactions specifically associated with the replication fork; and 4) examined for the induction of interstrand and intrastrand cross-links in DNA.

Identifying number: R01 CA 26379
Principal investigator: Brian A. Pethica
Institution: Clarkson College of Technology
Title: Dietary Fiber: The Physical Chemistry of Lignins

Total FY79 obligation: $113,315
Nutrition allotment: 100%
Nutrition funding: $113,315

Total FY80 obligation: $99,912
Nutrition allotment: 100%
Nutrition funding: $99,912

Cancer activity/thrust: Nutrition/Cause and Prevention

Dietary Fiber: The Physical Chemistry of Lignins (continued)

Project description:

Certain forms of cancer are believed to be less common when the diet contains fiber. The physiochemical properties of lignins will be examined in preparations partially or fully separated from plant fiber to provide a basis for hypothesis on the role of this constituent in the diet in relation to carcinogenesis. The binding of several carcinogens and cocarcinogens to these lignins will be studied. The main emphasis will be on nitrosamines and other nitroso compounds and bile salts. Lignin may also influence carcinogenesis through its oxidation-reduction properties, and through reaction with nitrites. It can also bind metal ions and other significant substances in the diet.

The study will illustrate the effect of lignin on the bioavailability of a variety of substances implicated in carcinogenesis.

Identifying number: R01 CA 26389
Principal investigator: Donald L. Hill
Institution: Southern Research Institute
Title: Disposition and Chemopreventive Activity of Retinoids

Total FY79 obligation: $143,960
Nutrition allotment: 100%
Nutrition funding: $143,960

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Retinoids are new drugs that can be used in the prevention of cancer of epithelial tissues. Since the tissue distribution and disposition of the synthetic members of this class of compounds is essentially unknown, this project will determine, by a sensitive procedure involving high-pressure liquid chromatography (HPLC), the blood levels and tissue distribution of 13-*cis*-retinoic acid, retinyl methyl ether, and *N*-2-hydroxyenthylretinamide in mice after oral and intravenous injections. All-*trans*-retinoic acid will be included as a control. The HPLC procedure uniquely allows determination of a variety of retinoids in many animal tissues.

For these four retinoids, it is planned to determine 1) the effect of inducers of mixed-function oxidases on their disposition in rats, 2) their subcellular distribution in responsive tissues, and 3) whether or not they accumulate in the livers of mice. The experiments are designed to elucidate any relationship between distribution of retinoids and their therapeutic effects. Such a relationship would be helpful in selection of the most appropriate retinoids for prevention of cancer in humans.

Identifying number: R01 CA 26412
Principal investigator: Lubomir S. Hnilica
Institution: Vanderbilt University
Title: Experimental Hepatocarcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $115,491
Nutrition allotment: 5%
Nutrition funding: $5,775

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The etiology and pathogenesis of malignant hepatomas will be studied with the help of cell and tissue specific markers. These markers are complexes of chromosomal nonhistone proteins with the DNA of the same species (homologous DNA). The complexes were shown to be immunologically cell and tissue specific. We propose to determine the biological and biochemical identities and functions of these markers. More specifically, we will characterize the protein and DNA components of these complexes and we will study their changes during the process of experimental hepatocarcinogenesis. Albino rats will be fed specific diets containing various carcinogens and the qualitative modifications of the chromatin and its components will be determined. Immediate effects of selected carcinogens (transformation) will be investigated in short-term experiments on tissue cultured hepatocytes derived from the livers of young and adult rat. . Using such cultures in context with the antigenic nonhistone protein-DNA markers, we will endeavor to develop a sensitive in vitro assay for carcinogenic chemicals.

Identifying number: R01 CA 26419
Principal investigator: Ilene L. Bernstein
Institution: University of Washington
Title: Learned Food Aversion: A Component of Cancer Anorexia

Total FY79 obligation: $56,276
Nutrition allotment: 100%
Nutrition funding: $56,276

Total FY80 obligation: $54,835
Nutrition allotment: 100%
Nutrition funding: $54,835

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The objective of this project is to evaluate the contribution of learned food aversions to the appetite and weight loss induced by tumors and antitumor therapy. These studies are based on recent demonstrations 1) that learned aversions to specific foods can occur in cancer patients receiving gastrointestinal toxic chemotherapy; and 2) that, in animals, tumor growth alone, in the absence of any aversive therapy, can produce aversions to the available diet.

With an experimental animal model, this project will 1) define the conditions under which aversions to foods are acquired as a consequence of tumor growth, and/or chemotherapy; 2) evaluate whether learned food aversions contribute to anorexia; and 3) evaluate intervention approaches for minimizing or eliminating these learned food aversions.

In the clinic it is planned to 1) continue to define the conditions under which learned food aversions are acquired as a consequence of gastrointestinal toxic chemotherapy as well as evaluate their impact on the nutritional status of cancer patients; and 2) evaluate the effectiveness of selected intervention methods in preventing learned food aversions in cancer patients receiving gastrointestinal toxic chemotherapy.

Identifying number: R01 CA 26513
Principal investigator: Calvin I. Long
Institution: Medical College of Ohio, Toledo
Title: Energy Metabolism in Cancer Patients

Total FY79 obligation: $95,038
Nutrition allotment: 100%
Nutrition funding: $95,038

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

This project is designed to quantitatively evaluate energy expenditure and the composition of the fuel mixture burned in patients with gastrointestinal cancer. In addition, glucose kinetics (oxidation rates, pool sizes, turnover rates, and recycling) will be measured with the use of ^{14}C-U-L-glucose, the degree of gluconeogenesis will be measured with the use of ^{14}C-L-alanine, and whole-body protein synthesis and catabolic rates will be measured with the use of ^{15}N-L-alanine.

These kinetic studies will be done at the beginning of the patient's hospital stay and during nutritional support before and after surgical removal of the tumor. Nutritional support will be high fat-low carbohydrate or high carbohydrate-low fat diet with constant protein composition.

The data should provide information on energy and substrate demands of the host and of the tumor by comparing the initial study (postabsorptive) with the preoperative study during nutritional support. Compartmentalization of the host-to-tumor demands may be ascertained by comparing the results before and after surgical removal of the tumor employing the same nutritional intake baseline in both studies. The postoperative study will be conducted only when the surgical catabolic transients are absent, which will be confirmed by a number of measured responses.

These studies are designed to provide additional information related to the amount and kind of nutritional support cancer patients should receive in their total care.

Identifying number: R01 CA 26515
Principal investigator: Laurence N. Kolonel
Institution: University of Hawaii, Manoa
Title: Case-Control Study of Lung Cancer and Dietary Vitamin A

Total FY79 obligation: $98,080
Nutrition allotment: 100%
Nutrition funding: $98,080

Total FY80 obligation: $74,828
Nutrition allotment: 100%
Nutrition funding: $74,828

Case-Control Study of Lung Cancer and Dietary Vitamin A (continued)

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This case-control study will test the hypothesis that dietary vitamin A may be protective against the development of lung cancer.

The multiethnic population of Hawaii, with its dietary heterogeneity, will be used to interview 500 newly diagnosed patients with primary lung cancer. These patients will be identified through the seven major hospitals on Oahu and will be men and women of Japanese, Caucasian, Filipino, Chinese, and Hawaiian ethnic groups. For each lung cancer patient, two age- and sex-matched controls will be identified with the use of the random-digit dialing method. Both patients and controls will be interviewed in their homes by trained multilingual interviewers, with the use of a questionnaire designed to elicit quantitative information on the consumption of a large number of dietary items containing preformed vitamin A and vitamin A precursors. A detailed history of smoking and exposure to occupational lung carcinogens will also be included in the questionnaire.

The data will be analyzed to determine the dietary vitamin A consumption of patients and controls with adjustment for smoking and occupational history. Further analysis will determine the dietary vitamin A consumption of cigarette-smoking patients versus cigarette-smoking controls with adjustment for covariates.

The demonstration of a relatively low dietary vitamin A intake among lung cancer patients, particularly among those who are smokers, would suggest that the incidence of this very common cancer might be reduced by increases in vitamin intake.

Identifying number: R01 CA 26532
Principal investigator: William L. Banks, Jr.
Institution: Virginia Commonwealth University
Title: Essential Amino Acid Nutrition and Mouse Tumor Growth

Total FY79 obligation: N/A

Total FY80 obligation: $73,362
Nutrition allotment: 100%
Nutrition funding: $73,362

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The studies proposed in this application are directed toward establishing the nutrient level(s) of essential amino acid(s) that will prevent tumor growth both in vitro and in vivo of four murine tumor models. These include the A26 glioma, Lewis lung carcinoma, MCA 2182 fibrosarcoma and B16 melanoma. By varying the level of each of the nine essential amino acids in the nutrient media, we expect to be able to identify those essential amino acids that are critical for the growth of each model system in vitro. Based upon these findings, we will establish the dietary level of those essential amino acids in vivo that will prevent tumor growth without compromising the host and produce prolonged survival. Moreover, we will determine the effects of nutrient restriction of essential amino acids on their transport and other metabolic parameters in vitro and in vivo. In addition, we will ascertain whether dietary essential amino acid restriction will prevent metastasis. Finally, we will establish whether the dietary essential amino acid restriction will have the same effects on each of several cloned lines of a single methylcholanthrene fibrosarcoma in order to determine whether or not tumor heterogeneity is expressed at the level of amino acid requirements.

Identifying number: R01 CA 26533
Principal investigator: Gary G. Meadows
Institution: Washington State University
Title: Nutritional Approach to Melanoma Treatment

Total FY79 obligation: $56,934
Nutrition allotment: 100%
Nutrition funding: $56,934

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

This research project deals with nutritional requirements for growth of B-16 melanoma. Dietary intake of tyrosine, phenylalanine, and cysteine will be correlated with establishment of tumors and with treatment of established tumors in mice. Special amino acid diets containing a specified amount of the amino acid(s) in question will be fed to tumor-bearing BDF_1 female mice. The antitumor effect of L-dopamethylester and carbidopa in combination with various nutritional manipulations of these amino acids will also be studied.

Nutritional Approach to Melanoma Treatment (continued)

The effect of the various treatments on life span in mice with ascites tumors will be determined and the effect of these treatments on the growth rate and survival of mice with subcutaneous tumors will be determined. The experiments with cysteine diets will provide information regarding the mechanism of action of L-dopamethylester in melanoma. Competition for uptake between tyrosine, phenylalanine, and ^{3}H-L dopamethylester will be determined by measuring the incorporation of radioactivity into melanoma tumors and melanin with the use of liquid scintillation counting.

Identifying number: R01 CA 26547
Principal investigator: Ervin J. Hawrylewicz
Institution: Mercy Hospital and Medical Center
Title: Effect of Diet on the Hypothalamus and Breast Tumors

Total FY79 obligation: $77,400
Nutrition allotment: 100%
Nutrition funding: $77,400

Total FY80 obligation: $95,038
Nutrition allotment: 100%
Nutrition funding: $95,038

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The program will evaluate the effect of several diets on the neurotransmitter-hormone relationship and its subsequent effect on mammary tumor genesis and growth.

The effect of varied protein-fat diets fed throughout the period of fetal, neonatal, and adult development on DMBA-induced, prolactin-dependent, rat mammary tumors will be determined. The diets are designed as high protein (28 percent), moderately high fat (15 percent) or low protein (8 percent), moderately high fat (15 percent) and compared to normal levels. The effect of these diets, fed throughout the neonatal period and after tumor induction, on the catecholamine and serotonin activity in specific hypothalamic nuclei will be determined. Serum prolactin and estradiol will be determined at concomitant test periods.

Tumors will be evaluated morphologically and the rate of DNA [^{3}H]thymidine and protein [^{3}H]leucine synthesis determined. Non-tumor-bearing animals will be assessed for the same neurotransmitters and hormones and compared with tumor-responding animals in the same dietary group.

Identifying number: R01 CA 26556
Principal investigator: Hisashi Shinozuka
Institution: University of Pittsburgh
Title: Diet Modification Promotion of Liver Carcinogenesis

Total FY79 obligation: $57,998
Nutrition allotment: 100%
Nutrition funding: $57,998

Total FY80 obligation: $91,587
Nutrition allotment: 100%
Nutrition funding: $91,587

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

A striking enhancement of hepatoma induction by several chemicals has been demonstrated in rats fed a diet devoid of choline. Several lines of experimental observations lend support to the promoting effects of a choline-devoid (CD) diet.

With the use of the initiation-promotion scheme of liver carcinogenesis, the role of a CD diet on promotion of carcinogenesis will be studied. Cellular analysis of progression of foci of initiated hepatocytes to hepatoma, under the influence of a CD diet or a non-CD diet, will be undertaken to determine their reversibility and to identify the phenotypic alterations that may occur during the course of the progression. Selected aspects of the mechanism of tumor promotion in the liver by a CD diet will be investigated, including the effects of the diet on liver cell proliferation and on liver cell differentiation.

These studies will provide a foundation for future studies concerning the cellular and biochemical basis of the modification of the carcinogenic process induced by other dietary components.

Identifying number: R01 CA 26557
Principal investigator: Herschel Sidransky
Institution: George Washington University
Title: Nutritional Influence on Chemical Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $75,332
Nutrition allotment: 100%
Nutrition funding: $75,332

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objectives of this proposal are to determine whether a certain dietary component, specifically L-tryptophan, may act as an inhibitor and/or a promoter in chemical carcinogenesis. Chemical carcinogens such as N-2-fluorenylacetamide, ethionine, and 3'-methyl-dimethylaminoazobenzene will be used. The effects of feeding purified diets containing single chemical carcinogens and elevated levels (1 percent) of L-tryptophan will be determined. Liver and urinary bladder will be evaluated for tumorigenesis and for selected enzyme changes.

Identifying number: R01 CA 26560
Principal investigator: Frank E. Speizer
Institution: Peter Bent Brigham Hospital
Title: Prospective Study of Diet and Cancer in Women

Total FY79 obligation: $125,592
Nutrition allotment: 100%
Nutrition funding: $125,592

Total FY80 obligation: $142,686
Nutrition allotment: 100%
Nutrition funding: $142,686

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This study is designed to address questions regarding the possible association between the intake of various dietary components and cancer of the breast and large bowel, as well as other diseases. This is to be done by taking advantage of an existing prospective study of risk factors for breast cancer in 121,000 women who complete a mail questionnaire on a biennial basis. This investigation will require the development of a short dietary questionnaire, administration of this questionnaire to the entire cohort, and subsequent followup on a biennial basis to gather data on the development of specific cancers of interest.

The questionnaire will be designed to provide relative scores for individuals on the intake of animal fat, vegetable fat, cholesterol, protein, fiber, vitamin A, and trans fatty acids. Data on potential confounding factors, including physical activity, for risk of breast cancer and large bowel cancer are being collected and will be controlled by multiple logistic analyses. To validate the questionnaire, 200 subjects will complete detailed 7-day food use diaries four times over a 1-year period. Blood specimens from 400 women at the extremes of consumption histories will be assessed for lipids, carotene, and vitamin A levels. These specimens will be preserved for possible subsequent endocrinologic determinations.

Outcome measures will include incidence rates for both fatal and nonfatal cancer. Reported cases of cancer will be documented by obtaining copies of hospital records and causes of death will be obtained from death certificates as well as hospital records.

Over the course of 4 years of followup, sufficient cases of cancer of the breast and large bowel are expected to occur on the cohort to permit a better than 90 percent chance of detecting a 1.5-fold risk for breast cancer and a twofold risk of cancer of the large bowel.

Identifying number: R01 CA 26563
Principal investigator: David Heber
Institution: UCLA Medical Center
Title: Enteral Supplements and Protein Metabolism in Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $103,434
Nutrition allotment: 100%
Nutrition funding: $103,434

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The role of enteral nutritional supplements in the prevention and treatment of protein-calorie malnutrition in cancer is not established. This study will examine the efficacy of enteral nutritional supplementation in preventing or reducing the progression of protein-calorie malnutrition in lung cancer patients utilizing a randomized prospective clinical design, a control population, and a single preselected treatment regimen. Patients with unresectable bronchogenic carcinoma with chronic lung disease prior to the development of severe protein-calorie malnutrition, based on weight status, performance status, and clinical characteristics, will be randomly assigned to control (group A) and enteral supplemented (group B) groups. Two groups of patients with chronic lung disease and no evidence of cancer will be matched carefully to each cancer patient and serve as controls in supplemented (group D) and control (group C) groups. Patients from all groups will be studied under metabolic ward conditions to determine basal energy expenditure, hormonal status, and multiple aspects of carbohydrate and protein metabolism. Estimated protein and calorie requirements will be supplied via carefully designed standard diets to all groups. Groups B and D from the cancer control populations will receive outpatient enteral supplementation designed to provide a 25 percent caloric supplement above basal requirements. Patients from all groups will be studied under metabolic ward conditions every 2 months and biweekly as outpatients. The effects of enteral supplementation on chemotherapeutic drug disposition and standard drug-related toxicity and response criteria will be examined. Outpatient and inpatient data will be compared. Based on a careful analysis of all the data, both the efficacy of this regimen of nutritional treatment and specific hormonal and metabolic aberrations will be examined, which may define a pattern of nutritional disease amenable to therapeutic intervention with specific hormonal, metabolic and nutritional therapies aimed at preventing, reversing, or treating the progression of protein-calorie malnutrition in patients with unresectable bronchogenic carcinoma.

Identifying number: R01 CA 26571
Principal investigator: Michael L. Simenhoff
Institution: Thomas Jefferson University
Title: In Vivo Nitrosamines and Cancer in Renal Failure

Total FY79 obligation: $185,519
Nutrition allotment: 30%
Nutrition funding: $55,656

Total FY80 obligation: $6,450
Nutrition allotment: 30%
Nutrition funding: $1,935

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

N-nitroso compounds (nitrosamines) are potent mutagens and carcinogens in experimental animals. Although no role has been determined in humans, studies of amine generation in chronic renal failure indicate that a human model may be found in uremic patients. This model describes the coexistence of three conditions for nitrosamine formation: 1) intestinal nitrates (nitrites) endogenous and exogenous (in food and water, including dialysate); 2) small intestinal secondary amines, especially dimethylamine (DMA); and 3) appropriate bacterial species in same location permitting reduction of nitrate and possibly nitrosation itself at physiologic pH and high temperatures.

Identifying number: R01 CA 26576
Principal investigator: James I. Gray
Institution: Michigan State University
Title: Formation of N-Nitroso Compounds in Processed Food

Total FY79 obligation: $64,554
Nutrition allotment: 100%
Nutrition funding: $64,554

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Carcinogenic N-nitroso compounds may be formed in foods as a result of the reaction between amines and nitrite. Although most previous studies have focused on the formation of the volatile N-nitrosamines, this group may constitute only a small proportion of the N-nitroso compounds to which humans are exposed. It is therefore important to establish whether other N-nitroso compounds or their precursors are formed as a consequence of the processing, cooking, or storage of foods. Conditions whereby such compounds may arise include the interaction of amino acids and amines with fatty acids, the interaction between oxidizing lipids and free amino compounds, and the thermal processing of foods containing large amounts of phospholipids.

The principal objectives of this research are to study with model systems and then with special food systems including meat, cheese, milk, and dried egg products, the conditions which contribute to the formation and occurrence of N-nitroso compounds or their precursors in food systems and to evaluate the effects of various methods of thermal processing (spray drying, drum drying, pasteurization) and cooking (by frying, broiling, microwave) on the formation of such compounds.

Formation of N-Nitroso Compounds in Processed Food (continued)

These compounds will be isolated, purified, and identified by chromatographic techniques with confirmation by mass spectrometry. The mutagenicity of these purified N-nitroso compounds will be evaluated with the use of the Salmonella typhimurium assay.

Identifying number: R01 CA 26586
Principal investigator: Albert Y. Sun
Institution: University of Missouri, Columbia
Title: Chlorinated Water and Membrane Functions and Neoplasia

Total FY79 obligation: $90,463
Nutrition allotment: 75%
Nutrition funding: $67,847

Total FY80 obligation: $69,793
Nutrition allotment: 75%
Nutrition funding: $49,345

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The interaction of chlorine and/or chlorinated compounds with some major body constituents of the rat such as proteins, lipids, nucleic acids, and nucleotides at the cellular and subcellular level will be investigated after administration of ^{36}Cl-labeled hypochlorite by gastric intubation. In addition, the inhibitory effect of dietary vitamin E and selenium on the chemical carcinogenesis will be evaluated.

Identifying number: R01 CA 26594
Principal investigator: Bill D. Roebuck
Institution: Dartmouth College
Title: Modulation of Pancreatic Carcinogenesis by Diet

Total FY79 obligation: N/A

Total FY80 obligation: $55,607
Nutrition allotment: 100%
Nutrition funding: $55,607

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Preliminary data indicate that high dietary levels (20 percent by weight) of unsaturated fat act to enhance the incidence, and the mean number of tumors per pancreas, as well as the severity of the pancreatic tumors in azaserine-treated, male Wistar/Lewis rats. Azaserine is a known pancreatic carcinogen for this rat. Comparable levels of saturated dietary fats do not enhance azaserine-induced pancreatic tumors. The enhancement appears to be a clearcut example of tumor promotion. This effect is demonstrated to occur when the rats are initiated with azaserine as well as during the postinitiation phase (during which no further carcinogen is given) when rats are fed high levels of dietary fat.

The objectives of these studies are to generalize the above very specific observation and, in doing so, to develop an understanding for the biochemical mechanism(s) of dietary promotion of pancreatic carcinogenesis. The proposed studies are to: 1) demonstrate that high dietary levels of unsaturated fat will promote pancreatic cancer in the established hamster model; 2) develop short-term (ca. 4 month) animal models for dietary promotion to circumvent the present expensive, time-consuming 1-year rat model; 3) apply some of the biochemical parameters thought to be indicative of promotion in the mouse skin system and the rat liver system to dietary promotion of pancreatic cancer; and 4) investigate, hopefully by a short-term model, unsaturated fat promotion of other pancreatic carcinogens, other possible promoting agents in the initiated pancreas, and dietary promotion in the opposite sex of the established model (i.e., female rat and male hamster).

Identifying number: R01 CA 26597
Principal investigator: Thomas Dao
Institution: Roswell Park Memorial Institute
Title: Dietary Fat and Mammary Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $118,333
Nutrition allotment: 100%
Nutrition funding: $118,333

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This research project will demonstrate conclusively the effects of a high fat diet on the induction of mammary cancers in three strains of rats. The possible cocarcinogenic effect of a high fat diet in mammary

Dietary Fat and Mammary Carcinogenesis (continued)

cancer induction by a chemical carcinogen will be defined. The possibility that high dietary fat alters the susceptibility of the mammary gland to carcinogenesis as related to the age of the host, the rate of mammary cell proliferation and hormone biosynthesis will be investigated by studying whether a high fat diet may increase the incidence of mammary cancer in postpubertal rats; by examining whether a high fat diet accelerates the rate of DNA synthesis and cell proliferation; and by measuring the biosynthesis of steroid and polypeptide hormones. The possible relationship between increased hormone production and increased rate of mammary cell proliferation in rats ingesting a high fat diet may be delineated. A comparison of the efficacy of polyunsaturated and unsaturated fat in their cocarcinogenic effect may lead to the identification of the type of fatty acid in the high-fat diet that enhances mammary tumorigenesis. An alternate hypothesis--that the amount of dietary fat consumed, rather than the specific type of dietary fat, plays a critical role in influencing the induction of mammary carcinogenesis--will also be tested.

Identifying number: R01 CA 26604
Principal investigator: Laurence M. Corwin
Institution: Boston University
Title: Effect of Vitamin E and Lipids on Tumorigenicity

Total FY79 obligation: $83,903
Nutrition allotment: 100%
Nutrition funding: $83,903

Total FY80 obligation: $81,480
Nutrition allotment: 100%
Nutrition funding: $81,480

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The major goal is to test the effect of varying doses of dietary vitamin E on the tumorigenicity of established tumor cell lines. Inasmuch as the influence of vitamin E is often modified by the presence of polyunsaturated fatty acids (PUFA), the titration of vitamin E will be against a background of different levels of dietary PUFA.

The impetus for this work has been the observation that it is possible to isolate a tumor cell variant whose tumorigenicity is relatively insensitive to changes in dietary fat compared with the original tumor cell line. This variant was isolated by growth in cell culture media depleted in lipids.

It was found that in mice fed a diet containing 4 percent lard the original tumor cell line was least tumorigenic when moderate levels of vitamin E were included in the diet relative to that seen with either high levels of vitamin E or none. The variety was unaffected by these dietary alterations. Given these otherwise isogenic strains, it would appear that they offer an excellent model to investigate the mode of action of fats and vitamin E on tumorigenicity.

Since tumorigenicity can be affected by tumor growth rate and the host's defense mechanisms, this study will include the effect of vitamin E in diets varying in PUFA levels on tumor growth, the host's immune response to tumors, and the susceptibility of the tumor cells to these defense mechanisms.

It is expected that this approach in an animal model will produce information useful in determining whether megadose levels of vitamin E or other lipid alterations in the diet can lower the incidence of cancer.

Identifying number: R01 CA 26606
Principal investigator: Lyle L. Sensenbrenner
Institution: Johns Hopkins University
Title: Influence of Nutrition After Cancer Therapy

Total FY79 obligation: $90,463
Nutrition allotment: 100%
Nutrition funding: $90,463

Total FY80 obligation: $92,807
Nutrition allotment: 100%
Nutrition funding: $92,807

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

Although many studies of chronic protein deprivation have been carried out, very little has been done with regard to the effect of acute short-term periods of protein deprivation on the ability of a lymphohematopoietic system injured by systemic cancer therapy to repair and restore itself.

Preliminary studies of the ability of transplanted bone marrow to repopulate a lethally irradiated mouse have clearly demonstrated that in the presence of no protein intake, there is marked prolongation and suppression of full engraftment of that transplanted marrow.

These studies will examine the quantitative effect of graded doses of dietary protein to restore normal repopulation kinetics of transplanted bone marrow. Studies will also be done to examine quantitatively the effect of graded amounts of dietary protein on the ability of autologous residual bone marrow CFUs and CFUc to restore and repopulate the mouse after sublethal systemic chemotherapy and irradiation. A quantitative determination will be made by the effect of those same protein-deficient diets on the ability of syngeneic immunocompetent cells to recover.

These studies will be extended to the study of the replicative ability of CFUs, CFUc, and their progeny from murine bone marrow cultured in diffusion chambers implanted into mice maintained for a short time on graded protein diets. Marrow from normal humans and patients with leukemia in varying states of remission and relapse will be grown in diffusion chambers implanted into mice treated with chemotherapy and/or radiation. These mice will be subjected to dietary deprivation post chamber implantation. At each of several times during culture, the effect of this deprivation on the chamber total and differential cell count, as well as the content of CFUc, will be determined.

Identifying number: R01 CA 26628
Principal investigator: Roy S. Weiner
Institution: University of Florida
Title: Effective Cancer Therapy With Nutritional Support

Total FY79 obligation: $114,315
Nutrition allotment: 100%
Nutrition funding: $114,315

Total FY80 obligation: $130,415
Nutrition allotment: 100%
Nutrition funding: $130,415

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

This prospective, randomized clinical trial of nutritional support will utilize a uniform, intensive combination chemotherapy regimen for induction of remission in patients with extensive oat-cell lung cancer.

The effects of intensive chemotherapy alone or with nutritional repletion will be measured in terms of 1) tumor response, 2) hematologic and immunologic tolerance to chemotherapy, 3) response in clinical parameters of nutritional status, 4) response in metabolic balance studies, and 5) response in lean body mass by ^{40}K measurements in a whole-body counter. Sequential quantification of cell-mediated immunity and hematopoietic function by in vitro assays of cell-mediated lympholysis and of granulocyte progenitor cells (CFU-C) in the peripheral blood will establish the effect of nutritional repletion on T-cell and hematopoietic stem cell function. Laboratory and clinical data will be collected over 2 months of intensive therapy on sufficient numbers of patients to establish significant correlation between clinical response and quantitative assays on physiology and function.

This project will define the role of adjunctive nutritional support of patients undergoing intensive anticancer therapy and will study the biochemical, metabolic, and cellular mechanisms by which nutrition and anticancer therapy interact.

Identifying number: R01 CA 26642
Principal investigator: Alexandra von der Decken
Institution: The Wenner-Gren Institute for Experimental Biology
Stockholm, Sweden
Title: Protein Nutrition and Primary Action of a Carcinogen

Total FY79 obligation: $30,420
Nutrition allotment: 100%
Nutrition funding: $30,420

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Nitroso compounds show great versatility as carcinogenic agents. Knowledge concerning protection by diet from the carcinogenic action of nitroso compounds is of great interest in relation to carcinogenesis in humans.

The aim of this investigation is to study the effect of administration of dimethylnitrosamine in mice fed a diet balanced in amino acids, or proteins enriched in sulfur-containing amino acids. The dietary conditions used will include high-quality proteins at a 20 percent level and enrichment of the proteins with the sulfur-containing amino acids, methionine and cysteine. These are introduced to test the theory that a reaction of the sulfur groups with dimethylnitrosamine intermediates will prevent interaction with the susceptible DNA molecules. The objective is to follow the protective influence such a diet has on the occurrence of single strand breaks in DNA caused by dimethylnitrosamine.

Protein Nutrition and Primary Action of a Carcinogen (continued)

Quantitation of the breaks produced in DNA will be done by labeling with ^{125}I followed by separation of the denatured DNA on polyacrylamide gel electrophoresis and autoradiography. Labeling of DNA at the break points with ^{32}P-ATP and polynucleotide kinase (EC 2.7.1.78) will also be tested. DNA will be labeled at the free 5'OH group with ^{32}P and, after separation by polyacrylamide gel electrophoresis, radioactivity will be determined. A further step is formation of initiation complex for DNA synthesis with Escherichia coli, RNA polymerase containing sigma factor (EC 2.7.7.6), and ^{32}P-ATP or ^{32}P-GTP as the initiation nucleotide. These may be replaced by ATP or GTP labeled with ^{14}C or ^{3}H. The heparin-resistant complex is precipitated, excess of radioactivity removed, and the remaining radioactivity determined. An unspecific initiation occurs in vitro at each single strand break.

Identifying number: R01 CA 26647
Principal investigator: Guylyn R. Warren
Institution: Montana State University
Title: Mutagenic/Carcinogenic Agents in Body Fluids of Children

Total FY79 obligation: N/A

Total FY80 obligation: $84,814
Nutrition allotment: 50%
Nutrition funding: $42,407

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Initial research by our group has demonstrated that children in the 3rd and 4th grades in Butte, Montana (Silver Bow County) excrete mutagenic substance(s) in urine samples taken during the school day. Mutagens have also been extracted from air filter samples taken in the area at the same time. The population of Silver Bow County has been shown to be at higher risk of dying of lung cancer than the national average in a state of lower than normal mortality and the town of Butte contains over 90 percent of the population of that county. This investigation will determine the number of children excreting mutagen(s) in Butte by using rapid mutagen assays of column concentrates, especially the Ames Salmonella assay, E. coli repair assay, Saccharomyces mutation and gene conversion assays. Selected positive and negative urine samples will also be assayed by CHO cell sister chromatid exchange and unscheduled DNA synthesis as well as mammalian cell forward mutation assay. Data will also be obtained on the relative sensitivities and efficacies of the short-term assays and on necessary statistical parameters of testing. Any mutagenic metabolites excreted by children will then be collected, pooled, isolated and characterized using thin layer chromatography, solvent extraction procedures and any other necessary isolation techniques and microbial tests. Air filter samples and water samples from the area where the children live will be assayed by the same techniques and the isolated mutagenic components will be compared chemically with those from urine samples. If no correspondence is found, dietary sources of mutagens will be investigated through both chemical analysis and interview data. We will identify the source(s) of mutagens with the purpose of being able to limit exposure of these children and to make their families aware of the possible risks. In this analysis synergism and antagonism in mixtures is amenable to investigation since fractions from urine samples and filter extracts will be available for mixing.

Identifying number: R01 CA 26716
Principal investigator: William A. Haseltine
Institution: Sidney Farber Cancer Institute
Title: DNA Damage/Repair by Environmental Carcinogens/Mutagens

Total FY79 obligation: $132,384
Nutrition allotment: 20%
Nutrition funding: $26,477

Total FY80 obligation: Active, not funded
Nutrition allotment: 20%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The goal of this research is to elucidate mechanisms whereby DNA lesions created by environmental (including dietary) agents are fixed into genetic lesions. Chemical carcinogens to be studied include aflatoxin B_1, safrole, benzo[*a*]pyrene, and acetylaminofluorine. The effect of certain forms of radiation, such as X rays, gamma rays, ultraviolet light, and microwaves will also be investigated.

Identifying number: R01 CA 26815
Principal investigator: Chih-Cheng Wang
Institution: Southern Research Institute
Title: Biotransformation of Retinoids in Vitro

Total FY79 obligation: N/A

Biotransformation of Retinoids in Vitro (continued)

Total FY80 obligation: $64,545
Nutrition allotment: 100%
Nutrition funding: $64,545

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Retinoids are new drugs that can be used in the prevention of cancer of epithelial tissues. The proposed research involves investigation of the microsome-dependent biotransformation of all-trans-retinoic acid, 13-cis-retinoic acid, all-trans-N-ethylretinamide and all-trans-N-(4-hydroxyphenyl)retinamide. The objectives of these studies are: 1) to assess the physiological significance of the interconversion of all-trans- and 13-cis-retinoic acids, 2) to determine the biological activity of the biotransformation products derived from all-trans-N-ethylretinamide and all-trans-N-(4-hydroxyphenyl)retinamide using organ culture, 3) to structurally identify the biotransformation products and 4) to characterize the microsome-associated catalytic agent. Most of the work will be performed with unlabelled retinoids. High-pressure liquid chromatography will be the method used to determine the levels of retinoids and their biotransformation products in biological samples.

Identifying number: R01 CA 26917
Principal investigator: Paul M. Newberne
Institution: Massachusetts Institute of Technology
Title: Dietary Fat in Colon Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $109,503
Nutrition allotment: 100%
Nutrition funding: $109,503

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Studies are proposed to determine the effects of dietary fats on chemical induction of colon tumors in rats and to evaluate the contribution of several different mechanisms by which diet may influence chemical carcinogenesis. Tumor incidence and latent period will be measured in male Sprague-Dawley rats fed 12 or 46 percent of calories as predominantly saturated (beef tallow), unsaturated (corn oil) or partially saturated (Crisco®) fat and treated with 1,2 dimethylhydrazine

(DMH) or N-methyl-N-nitrosourea (NMU). Possible mechanisms of dietary effects will be examined by quantitation of hepatic and colonic mucosal mixed function oxidase, cytochromes P-450 and P-448, NADPH cytochrome c reductase, cellular kinetics of colonic mucosa and humoral and cellular immunity and by examination of DMH metabolism in vivo and in vitro using rats treated by the same dietary and chemical methods. The results should confirm and extend knowledge of effects of dietary fat on colon tumor incidence and provide at least partial explanations of the means by which fat exerts its effect.

Identifying number: R01 CA 27324
Principal investigator: Richard Mandel
Institution: Boston University
Title: Additive and Synergistic Effects of Mutagens

Total FY79 obligation: $32,028
Nutrition allotment: 5%
Nutrition funding: $1,601

Total FY80 obligation: $48,838
Nutrition allotment: 5%
Nutrition funding: $2,441

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

It has been estimated that from 80 to 90 percent of all human cancers are caused by chemical carcinogens, many of which are present in the environment. Decisions regarding allowable levels of these environmental carcinogens are currently questionable because of uncertainty as to how these agents interact. The purpose of this project is to examine the additive and synergistic effects of pairs of carcinogens including aflatoxin B_1 and benzo[a]pyrene. An attempt will be made to establish criteria for understanding their combined effect.

Identifying number: R01 CA 27426
Principal investigator: Dennis P. Hsieh
Institution: University of California, Davis
Title: Comparative Toxicology of Carcinogenic Mycotoxins

Total FY79 obligation: $92,164
Nutrition allotment: 100%
Nutrition funding: $92,164

Comparative Toxicology of Carcinogenic Mycotoxins (continued)

Total FY80 obligation: $150,985
Nutrition allotment: 100%
Nutrition funding: $150,985

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Aflatoxin M_1 (AFM_1), a metabolite of the potent carcinogenic mycotoxin aflatoxin B_1, has been widely detected in the milk and edible tissues of animals exposed to AFB_1. Evidence has shown that AFM_1 is also a potent carcinogen. The objective of this research is to determine the carcinogenic activity of AFM_1, as compared to AFB_1, in mammalian species and to provide useful data to aid in the establishment of a realistic, rational, and valid tolerance level for AFM_1 in foods.

Identifying number: R01 CA 27564
Principal investigator: Robert M. Hoffman
Institution: University of California, San Diego
Title: Methionine Dependence: A Metabolic Marker in Cancer

Total FY79 obligation: $58,272
Nutrition allotment: 100%
Nutrition funding: $58,272

Total FY80 obligation: $101,172
Nutrition allotment: 100%
Nutrition funding: $101,172

Cancer activity/thrust: Nutrition/Cancer Biology

Project description:

This project will provide a better understanding of the biochemical basis of the requirement of many malignant and transformed cells for exogenous methionine (Met) despite high levels of endogenous Met synthesis from homocysteine (Hc).

In cells that are Met dependent (met^-) and independent (met^+), this project will kinetically study the formation of the cellular free Met pool from Met precursors as well as the utilization of Met from this pool to form the two major metabolites of Met, S-adenosylmethionine (SAM) and Met-tRNA. These studies will be done comparatively in met^+ normal human diploid cells, met^- transformed and malignant cells, and met^+ cells derived from them.

When met cells are incubated in Hc medium, they are reversibly growth arrested, possibly at the G_1/S border of the cell cycle, which will be further characterized with respect to position in cell cycle and which factors are rate limiting. In human cells, including normal human diploid fibroblasts, the biosynthesis of the two enzymes catalyzing the major reactions utilizing Met, methionine adenosyltransferase (MAT) and methionyl +RNA synthetase (MTS), are repressed by Met. In normal human diploid cells, MAT derepresses only in growing cells, not resting cells. In met cells endogenously synthesized, Met does not seem to repress MAT. The genetic regulation of these enzymes, their relation to growth control, and normal and altered cellular compartmentation of Met will be structured. The Met-dependence marker has been used in transformed and malignant cells to select met cells which have concomitantly reverted for properties of transformation including the first human transformation revertants.

These diverse revertants will be used to ascertain in collaborative studies with D. Livingston whether their properties correlate with various forms of SV40-specific T-antigen.

Identifying number: R01 CA 27594
Principal investigator: Young-Nam Cha
Institution: Johns Hopkins University
Title: Mechanism of Antimutagenesis by Anticarcinogens

Total FY79 obligation: N/A

Total FY80 obligation: $62,482
Nutrition allotment: 80%
Nutrition funding: $49,986

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Production of experimental tumors by a variety of chemical carcinogens may be inhibited by the administration of butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), ethoxyquin, selenium, and vitamin E (anticarcinogenic agents). Investigations in these and other laboratories have established that administration of BHA to rodents (1) protects a variety of target tissues against the production of tumors by a wide range of chemical carciogens, (2) reduces the levels of mutagenic metabolites from benzo(a)pyrene (BP) and numerous therapeutic agents, in vivo (antimutagenic), (3) elevates the hepatic levels of various enzymes involved in the detoxification of reactive metabolite and alters other hepatic enzymes and catalytic constituents (enzyme modifications), (4) increases the concentrations of nonprotein thiol compounds

Mechanism of Antimutagenesis by Anticarcinogens (continued)

in the liver and several other tissues. Utilizing these recently discovered principles and methodologies, we propose to study the biochemical mechanisms involved in the antimutagenic effects of the anticarcinogenic agents as a prerequisite for the design and development of more selective means to reduce or eliminate the mutagenic and carcinogenic potential of environmental chemicals. We shall compare the antimutagenic potencies of anticarcinogenic agents using two defined carcinogens (BP and acetylamino fluorine). The alterations in biochemical parameters caused by anticarcinogenic agents will be correlated also with their antimutagenic effects. Additionally, the production of various metabolites of the carcinogens will be analyzed in biological fluids by high pressure liquid chromatography and the mutagenic activity of these fractions will be determined.

Identifying number: R01 CA 27706
Principal investigator: Clement C. Ip
Institution: Roswell Park Memorial Institute
Title: Selenium Supplement and Dietary Fat in Breast Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $92,165
Nutrition allotment: 100%
Nutrition funding: $92,165

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objective of this research proposal is to determine the effect of dietary selenium supplementation on mammary carcinogenesis induced in rats by 7,12-dimethylbenz(a)anthracene (DMBA) with special emphasis on the ability of selenium to reduce the marked tumor incidence observed in rats fed a high fat diet. Our interest in selenium as a potential anticarcinogen stems primarily from its ability to protect against peroxidation. The lability of a given tissue to oxidative damage is a function of the balance between the concentration of polyunsaturated lipids and the antioxidant defense capacity. Thus uncontrolled lipid peroxidation may occur as a result of a high unsaturated fat intake and in the absence of an adequate supply of intracellular antioxidant. In this study, we will look into the effect of selenium status on the susceptibility of the mammary tissue to carcinogenesis and the lability of the tissue to lipid peroxidation in rats fed a high fat versus a low fat diet and in rats fed a saturated fat versus an unsaturated fat diet.

We are also interested in finding out whether additional vitamin E and methionine can enhance the efficacy of selenium in this regard, since these two compounds are known to potentiate the antioxidant status of the animal. In order to delineate if the action of selenium is distinct from other artificial antioxidants such as butylated hydroxytoluene, we will determine if the effects of selenium and BHT are additive in the inhibition of DMBA-induced mammary tumorigenesis. By supplementing the diet with selenium either before and after DMBA administration, we will also try to determine if selenium has any influence on DMBA metabolism. If we can conclusively demonstrate that low doses of selenium are effective in inhibiting the development of neoplastic diseases that are promoted by dietary fat, the use of selenium at nutritional levels can offer a potential means of cancer prevention.

Identifying number: R01 CA 27809
Principal investigator: Leonard A. Sauer
Institution: Mary Imogene Bassett Hospital
Title: Pathways of Energy Metabolism in Maligancy in Vivo

Total FY79 obligation: N/A

Total FY80 obligation: $55,654
Nutrition allotment: 100%
Nutrition funding: $55,654

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The amino acids and carbohydrates that are oxidized for energy are transported between the tissues and organs by well-defined interorgan transport cycles. In general, these cycles are arranged so that a metabolic product released from one organ is absorbed and oxidized by another. For example, glutamine released from skeletal muscle into the venous blood is absorbed and oxidized to CO_2 by the intestinal mucosa. Recent in vitro experiments have suggested that glutamine and the ketone bodies are the major respiratory fuels for fast-growing, undifferentiated tumors. Mitochondria from these tumors contain a kidney-type, phosphate-dependent glutaminase and an NAD(P)-dependent malic enzyme, the enzymes required for the net oxidation of glutamine, and succinyl CoA:acetoacetate CoA transferase, the enzyme necessary for ketone body oxidation. The activities of these enzymes are low in normal liver and the slow-growing hepatomas but high in fast-growing, undifferentiated hepatomas. Consequently, new enzyme synthesis occurs during tumor progression in hepatomas. We propose that a common pattern of substrate utilization for energy production is adopted by all undifferentiated tumors. The pattern is characterized

Pathways of Energy Metabolism in Maligancy in Vivo (continued)

by the oxidation of glutamine and ketone bodies as the major respiratory fuels. The objective of this research is to test this hypothesis in vivo using a series of transplanted hepatomas and other tumors of varying growth rates and degrees of transplanted hepatomas and other tumors of varying growth rates and degrees of differentiation. A clearer understanding of energy production in tumors, the changes in energy production that occur during tumor progression, and the interrelationship between tumor and host will result.

Identifying number: R01 CA 27831
Principal investigator: Henry T. Lynch
Institution: Creighton University
Title: Epidemiologic-Biologic Study of Colon Cancer Families

Total FY79 obligation: N/A

Total FY80 obligation: $308,726
Nutrition allotment: 20%
Nutrition funding: $61,745

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

We shall attempt to discriminate gene carriers from nongene carriers in the cancer family syndrome (four families) and in a family with hereditary site specific colon cancer on the basis of: (1) thymidine labeling of colonic epithelium; (2), growth characteristics of colonic epithelium cultured in vitro; (3) tetraploidy in cutaneous epithelium; (4) growth characteristics and viral transformation of cutaneous fibroblasts; (5) recognitive immunity in mixed lymphocyte culture; and (6) fecal cholesterol degradation products. These putative biomarkers of cancer susceptibility will be subjected to a biostatistical-genetic analysis utilizing maximum likelihood techniques in search for the marker or complex of markers most closely associated with cancer risk status in patients from these families.

We will also perform a genetic linkage analysis to determine if variation in these quantitative markers can be shown to be associated chromosomally with classical genetic markers. All statistical methods will be directed towards a substantive verification of the basis cancer genetics model proposed for these families and the usefulness of a biomarker index for identification of gene carriers.

Recognition of markers specific to the cancer prone genotype will have important implications for identification of high risk patients in the general asymptomatic population and will be of utility in the study of mechanisms of carcinogenesis.

Identifying number: R01 CA 27861
Principal investigator: Cosmo G. MacKenzie
Institution: University of Colorado Health Sciences Center
Title: A Nutritional Control of Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $74,560
Nutrition allotment: 100%
Nutrition funding: $74,560

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Cultured cancer cells exhibit a much higher arginine requirement that their normal counterparts with similar growth rates. Furthermore, when arginine is omitted from the medium, or arginase added, the cancer cells die sooner than normal cells. That a reduction in the arginine content of cancerous tissue may be a first line of defense against cancer in vivo is suggested by the discovery that macrophages, which are numerous in many solid cancers, synthesize and secrete large amounts of arginase. Since most dietary proteins are rich in arginine, it follows that the removal of arginine, and its major precursors, from an amino acid diet may be effective in retarding or abolishing the growth of cancer in living animals. Furthermore, this treatment can be supplemented by the addition to the diet of canavanine, which is not only a competitive antagonist of arginine, but also a destablizer of proteins, into which it is incorporated. In addition to these dietary approaches, we will simultaneously inject the experimental animals with homologous liver arginase; or, alternatively, with beef liver arginase whose antigenicity has been minimized by coupling with methoxypolyethylene glycol. Should arginine deprivation plus these supplementary treatments only arrest the growth of cancer cells without destroying them, a burst of mitotic activity will be produced by adding arginine to the diet and chemotherapeutic agents which are most destructive of dividing cells, such as methotrexate will be concomitantly administered. When used intermittently the latter procedure might well destroy all cancer cells, or at least minimize the often devastating effects of uninterrupted chemotherapy.

Identifying number: R01 CA 27917
Principal investigator: Morteza Janghorbani
Institution: Massachusetts Institute of Technology
Title: Dietary Bioavailability of Selenium in Man

Total FY79 obligation: N/A

Total FY80 obligation: $81,926
Nutrition allotment: 100%
Nutrition funding: $81,926

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Knowledge of dietary availability of selenium in man is limited due to lack of noninvasive experimental methods applicable to normal man. In this proposal, we will develop the method of stable (nonradioactive) isotope enrochment of the diet in connection with neutron activation analysis to permit accurate and nonhazardous measurement of selenium bioavailability in man. We will investigate, in pilot studies, various aspects of selenium absorption and excretory pathways in normal adults in order to demonstrate the feasibility of this noninvasive method in humans. We will compare bioavailability of three different forms of selenium (selenite, selenomethionine, and factor-III) by appropriately labeling with the stable selenium, ^{74}Se. Our long-term goal is to develop methods for the study of mineral bioavailability in all human subjects, including children and pregant women; and to understand in quantitative terms any relation between dietary availability of selenium and its role in etiology of diseases, especially cancers.

Identifying number: R01 CA 27934
Principal investigator: Carter J. Grandjean
Institution: Midwest Research Institute
Title: Diallylnitrosamine Carcinogenesis: Species Differences

Total FY79 obligation: N/A

Total FY80 obligation: $110,036
Nutrition allotment: 20%
Nutrition funding: $22,007

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

In general, nitrosamines constitute a class of potent carcinogens that induce tumors in all rodent species, although the tumor sites do vary between species. There are only a few examples of noncarcinogenic nitrosamines that are not fully substituted at the alpha-positions and hence prevent alpha-hydroxylation (activation). Diallylnitrosamine (DAN) is one such compound and was reported noncarcinogenic in the BD rat. However, we have found DAN to be a potent inducer of respiratory tract tumors in the Syrian golden hamster upon multiple or a single subcutaneous (s.c.) injection. These compartive findings give rise to multiple questions concerning this type of species difference never observed before with nitrosamines.

To determine some of the factors that may contribute to this dramatic species difference in light of the present knowledge about nitrosamine carcinogensis, the following studies are proposed: (1) determination of the carcinogenic response of the Syrian golder hamster and the BD(IX) rat to DAN using intragastric and subcutaneous administration; (2) determination of whether DAN is metabolically converted into other nitrosamines in either species using both i.g. and s.c. routes of administration; (3) determination of the qualitative and quantitative distribution of covalently bound adducts to nucleic acids in high and low risk tissues in the hamster and rat upon i.g. and s.c. administration of DAN-3H; (4) determination of the qualitative and quantitative persistence of specific alkylated components of nucleic acids in high and low risk tissues in both species, as determined from the proposed chronic animal testing.

Identifying number: R01 CA 27967
Principal investigator: Yogesh C. Awasthi
Institution: University of Texas Medical Branch at Galveston
Title: Mechanism of Anticarcinogenic Effect of Antioxidants

Total FY79 obligation: N/A

Total FY80 obligation: $46,486
Nutrition allotment: 100%
Nutrition funding: $46,486

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The antioxidants such as t-butylhydroxyanisole, t-butylhydroxytoluene, and ethoxyquin offer protection to mice from lung adenoma and other forms of cancer caused by the administration of benzo(*a*)pyrene (BP) and dibenz(*a*, *h*)anthracene (DBA). However, the mechanism of this protection is not clear. The anticarcinogenic effect of antioxidants could either be due to the activation of the enzyme systems (such as GSH-S-transferases) which are involved in the detoxification of highly electrophylic toxic metabolites of procarcinogens or the Antioxidants

Mechanism of Anticarcinogenic Effect of Antioxidants (continued)

are themselves metabolized by mixed function oxidases in the same manner as the carcinogens and the metabolites of antioxidants compete with 'ultimate' carcinogens for the binding with cellular macromolecules. The work proposed in this project is aimed at understanding the mechanism of the effect of anticarcinogenic action of antioxidants. The effect of oral administration of ethoxyquin, BHA and BHT will be studied on lung adenoma produced in mice by administration of BP and DBA. The effect of those compounds on the total GSH-S-Transferase of the lung and on the isozymic pattern of this enzyme will be studied. Besides kinetic characterization, immunochemical studies will be performed using antibodies raised against homogenous preparations of genetically distinct mouse lung GSH-S-transferases. Since in the mouse liver several genetically distinct isozymes are known, the effect of antioxidants on each one of the GSH-S-transferase isozymes of lung will be studied. GSH-S-transferase is known to bind chemical carcinogens; therefore, the binding of each of the mouse lung GSH-S-transferase and the metabolites of BA and BP will be studied. In addition, the effect of antioxidants on the mixed function oxidases which are responsible for the activation of chemical carcinogens and on the overall metabolism of GSH which provides in vivo substrate (GSH) for GSH-S-transferase will be studied. Metabolism of antioxidants by mixed function oxidases will be studied by incubating the antioxidants with microsomal fraction and by characterizing the metabolites using modern physicochemical techniques. Effect of these metabolities on the binding of carcinogen and GSH-S-transferase will also be studied.

Identifying number: R01 CA 28006
Principal investigator: Lynn Astle
Institution: University of Utah
Title: Gastrointestinal Carcinogenicity of Malondialdehyde

Total FY79 obligation: N/A

Total FY80 obligation: $67,918
Nutrition allotment: 100%
Nutrition funding: $67,918

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Malondialdehyde (MDA) is found in modest amounts in meat and some other foods. Preliminary studies have implicated it as a mutagen and carcinogen. Studies will be conducted to determine its carcinogenicity when it is chronically administered orally or intrarectally in Sprague-Dawley rats for 1 year. In separate studies, rats will be maintained on diets of either rat chow, hamburger, wheat, rat chow plus 20 percent safflower oil, or rat chow plus 20 percent lard for 2 weeks and then sacrificed. The gastrointestinal contents will be assayed for MDA. Correlations between the dose response data from the carcinogenicity studies and the MDA content of the gastrointestinal tract will be attempted to give some estimate of the potential risk of dietary MDA carcinogenicity.

Identifying number: R01 CA 28109
Principal investigator: Henry J. Thompson
Institution: University of New Hampshire
Title: Nutrition and Mammary Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $69,975
Nutrition allotment: 100%
Nutrition funding: $69,975

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Studies are proposed to determine a nontoxic level and source of dietary selenium which affords maximal protection against 1-methyl-1-nitrosourea and 7,12-dimethylbenz(a)anthracene-induced mammary carcinogenesis. The inhibitory effect of selenium on the initiation and progression stages of carcinogenesis will be studied both in mammary gland organ culture and via feeding studies. The role of alterations in both the metabolism of steroid sex hormones and the synthesis of DNA and protein will be investigated as possible mechanisms by which selenium exerts its effect. Additional studies will be conducted to answer questions pertinent to the application of selenium treatment to breast cancer control and prevention.

Identifying number: R01 CA 28140
Principal investigator: George P. Tryfiates
Institution: West Virginia University
Title: A Novel Vitamin B_6 Metabolite in Hepatomas

Total FY79 obligation: N/A

Total FY80 obligation: $48,084
Nutrition allotment: 100%
Nutrition funding: $48,084

A Novel Vitamin B_6 Metabolite in Hepatomas (continued)

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

During the course of preliminary experiments regarding the metabolic transformations of tritiated pyridoxine (PN) in animals with transplantable hepatomas, we observed a novel labeled vitamin B_6 metabolite peculiar to hepatomas. In these tests, uniformly labeled PN was administered intraperitoneally to control and tumor-bearing rats, and the metabolic transformations of the vitamin were studied in liver and the hepatomas. Rats were killed at different time intervals following label injection, livers and tumors removed and vitamin metabolites isolated from homogenates using acid extraction. The labeled metabolites were chromatographically separated on Dowex-H plus-ion exchange columns using linear pH gradient elution. Vitamin B_6 standard compounds were also similarly chromatographed individually and also as mixtures. Further identification of each eluting peak was made using high voltage electrophoresis (Savant) and thin layer chromatography on silica gel (BBA 451, 333-341, 1976). The occurrence of a novel, radioactively labeled peak was observed only when extracts from hepatomas were chromatographed on Dowex columns. The labeled peak eluted before pyridoxal and after elution of the three phosphorylated vitamin B_6 forms. Further thin layer chromatography on silica gel showed that this novel labeled vitamin metabolite was not pyridoxic acid or any of the known vitamin B_6 compounds (i.e., pyridoxine, pyridoxal, pyridoxamine and their phosphorylated derivatives). For this application I propose experiments to identify and characterize this novel vitamin B_6 metabolite and assess its importance to the economy of the tumor cell. The proposed studies may well show a new vitamin B_6 metabolic pathway in tumor cells which may be mediated by an as yet unknown enzyme protein which would be characterized.

Identifying number: R01 CA 28234
Principal investigator: Richard F. Branda
Institution: University of Minnesota, Minneapolis-St. Paul
Title: Folate Metabolism in Blood and Bone Marrow Cells

Total FY79 obligation: N/A

Total FY80 obligation: $55,811
Nutrition allotment: 45%
Nutrition funding: $25,115

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

Membrane transport and intracellular metabolism of folate compounds have been extensively studied in bacteria and in animal cell lines, but these processes are poorly characterized in human cells. I suggest that a better understanding of these cellular functions might provide new insights into several clinical problems. For example, my preliminary work suggests that disorders of cellular folate metabolism, rather than simple vitamin deficiency, may cause or contribute to the hematologic abnormalities in some patients with preleukemic conditions such as aplasticanemia, sideroblastic anemia and erythremic myelosis. One objective of this proposed research is to identify these patients and characterize their cellular metabolic abnormality. Patients with these preleukemic conditions will be screened for evidence of impaired folate metabolism by measuring uptake of radiolabeled folate in erythrocytes, peripheral blood lymphocytes, and bone marrow cells. Identified patients will be studied in more detail for defects of membrane transport or intracellular utilization of the vitamin. Following treatment with high doses of folic acid, an attempt will be made to assess whether this therapy alters the risk of subsequent leukemic transformation. In conjunction with these patient studies, I plan to more fully characterize the membrane transport system for folate compounds in human cells, using erythrocytes as a model system. A better understanding of this cellular function may facilitate the design of more effective chemotherapeutic regimens utilizing folate antagonists. Finally, these studies may also provide new approaches to the treatment of malaria, since these intraerythrocytic parasites depend upon the host cell membrane for transport of nutrients. I intend to investigate the antimalarial activity of compounds which inhibit the membrane transport of folate compounds.

Identifying number: R01 CA 28242
Principal investigator: Harold Draper
Institution: University of Guelph
Title: Toxicity and Metabolism of Malonaldehyde

Total FY79 obligation: N/A

Total FY80 obligation: $46,675
Nutrition allotment: 100%
Nutrition funding: $46,675

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The acute and chronic toxicity of malonaldehyde (MA), a reportedly carcinogenic product of lipid peroxidation in foods and in vivo, will be evaluated in animals and in cell cultures. MA will be administered to Swiss female mice at levels of 0.1, 1.0 and 10.0 microgram/gram body

Toxicity and Metabolism of Malonaldehyde (continued)

weight/day for 1 year. Complete hematology and histopathology will be performed, with emphasis on liver, pancreas and bladder, in which nuclear changes were seen previously in mice given larger doses of MA for 92 days. All tissues will be examined for evidence of tumors, and selected organs will be analyzed for lipofuscin pigments. The acute oral LD50 and ND50 of MA will be determined in mice and rats.

Rat skin fibroblasts, rat hepatocytes, and human lymphocytes will be used to determine the effect of MA on cell and nuclear morphology, chromosome structure, nucleic acid metabolism and protein synthesis. The binding of 14C-MA by DNA, RNA, and protein will be investigated using pure compounds and cell cultures in an effort to determine the nature of the bonds formed with MA by these substances in vivo.

Previous studies on the metabolism of 14C-MA by rat liver mitochondria will be extended to elucidate more clearly the pathway of metabolism of this compound and to identify the intermediary products.

Identifying number: R01 CA 28263
Principal investigator: Frederick F. Becker
Institution: University of Texas
Title: Chromosomal Proteins in Chemical Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $89,120
Nutrition allotment: 50%
Nutrition funding: $44,560

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The chronic administration of many chemical agents results in the appearance of malignant tumors in target tissues. These malignancies are characterized by alterations in control of cellular functions which suggest that mechanisms of genetic modulation have been altered. Recent evidence has accumulated which suggests that nonhistone chromosomal proteins (NHCP) are involved in transcriptional control. The object of this proposal is to analyze these NHCP in normal liver, at well-delineated stages of carcinogenic evolution and in the tumors which arise. We will use our previously described, intermittent dietary regimen of acetylaminofluorene (AAF) and examine 1) liver exposed to subcarcinogenic doses, 2) the premalignant nodules which arise with further exposure, and 3) subsequent malignant tumors. Additionally, the effects of a chronic regimen of diethylnitrosamine (DEN) will be evaluated. The effect of a single dose of DEN along or in conjunction with partial hepatectomy and combination regimens consisting of short exposure to DEN or AAF followed by phenobarbital will be similarly studied. Cytosol, nuclei, and chromatin will be isolated, purified, and their proteins analyzed by isoelectric focusing followed by SDS-electrophoresis in the recently developed Iso-Dalt System. This system allows for the simultaneous resolution of 20 individual protein samples thereby eliminating electrophoretic variance due to casting gels individually, multiple buffer preparations, and/or slight variance in power supply performance. The resulting electropherograms will be analyzed quantitatively and qualitatively to detect possible proteins uniquely associated with the carcinogenic process.

Identifying number: R01 CA 28287
Principal investigator: Thomas C. Smith
Institution: University of Texas Health Science Center, San Antonio
Title: Driving Forces for Nutrient Transport in Tumor Cells

Total FY79 obligation: N/A

Total FY80 obligation: $42,538
Nutrition allotment: 100%
Nutrition funding: $42,538

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The "Na ion gradient hypothesis" proposes that in animal cells the electrochemical potential gradient for Na ion, which is established by active Na/K transport, serves as the sole energy source for driving accumulation of certain organic solutes by the cell. The major controversy about this postulate is the adequacy of the energy available from the cation gradients to energize the entire amino acid uptake.

This proposal is based on the hypothesis that the cell membrane potential plays an essential role in both the regulation of cellular electrolyte activity and the provision of nutrients necessary for cellular metabolism. The long-range goal of the project is to characterize the role of the membrane potential as an important component of nutrient uptake, and in particular amino acid transport, essentially for maintenance of cell integrity and growth. To accomplish this objective, we will investigate in Ehrlich ascites tumor cells: 1) the effect of amino acid transport on the cell membrane potential; 2) the effects of amino acids on the intracellular Na ion and K ion electrochemical activity; 3) the coupling stoichiometry of cation-amino acid co-transport; and 4) how experimental alterations of the membrane potential affect amino acid transport. Membrane potential and cytoplasmic cation activities will be measured with intracellular glass microelectrodes.

Driving Forces for Nutrient Transport in Tumor Cells (continued)

We anticipate that this investigation will define the role of the cell membrane potential in the regulation of amino acid movements and lead to a more complete understanding of the energetics involved in meeting the cell's nutritional requirements.

Identifying number: R01 CA 28340
Principal investigator: Alton Boynton
Institution: National Research Council of Canada
Title: Assays for, and Actions of, Carcinogens and Promoters

Total FY79 obligation: N/A

Total FY80 obligation: $51,051
Nutrition allotment: 100%
Nutrition funding: $51,051

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The extracellular calcium ion regulates a late stage of prereplicative development of nonneoplastic cells through a calcium, cyclic AMP, and cyclic AMP-dependent protein kinase mechanism. This calcium-cyclic AMP regulatory system is somehow altered in neoplastic cells because they need 50- to 100-fold less extracellular calcium to proliferate than nonneoplastic cells. We will test a wide variety of nonneoplastic and neoplastic cells for ther proliferative calcium requirements and correlate these requirements with their ability to grow in soft agar and to form tumors in athymic nude mice. We will exploit this difference between nonneoplastic and neoplastic cells by developing an assay for carcinogenic agents, in which transformed cells are selected by incubation in medium containing only 0.01 mM calcium. The blockage of nonneoplastic cells proliferation in low-calcium medium can be overcome by calcium or a variety of other agents which all seem to function by causing a brief cyclic AMP surge. Tumor-promoting agents (such as TPA, phenobarbitol and saccharin) can also replace calcium and just as rapidly (within 1 hour) stimulate DNA synthesis. This system suggests a rapid (48-72-hour) in vitro assay for tumor promoters. Experiments will also be performed to determine how tumor promoters affect the calcium, cyclic AMP, cyclic AMP-dependent protein kinase system.

Identifying number: R01 CA 28427
Principal investigator: Eileen D. Adamson
Institution: La Jolla Cancer Research Foundation
Title: EGF and Its Receptors in Embryonic Differentiation

Total FY79 obligation: N/A

Total FY80 obligation: $115,159
Nutrition allotment: 5%
Nutrition funding: $5,758

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The role of epidermal growth factor (EGF) and its receptors (EGF-R) during embryonic development and during the differentiation and loss of tumorigenicity of teratocarcinoma cells will be studied.

Epidermal growth factor receptors have been demonstrated on the cell surface of certain differentiated teratocarcinoma cell lines. Undifferentiated embryonal carcinoma (EC) cells are malignant and totipotent, but their differentiated cell products have little or no tumorigenicity. The former cells do not have significant numbers of 125I-EGF binding sites and the hypothesis is that in the teratocarcinoma system, growth control may be governed by EGF and its receptors (EGF-R). In many respects, teratocarcinoma cells are a model of mouse development, and this suggests that the tissues of the mouse may become subject to growth control during development either by a) the appearance of EGF-R and maternal EGF or by b) the synthesis of EGF as well as EGF-R. Other markers of endoderm differentiation will be alpha-fetoprotein, transferrin, and basement membrane collagens.

It is intended to study the first appearance and the distribution of EGF-R in mouse embryos using labeled EGF. Further studies of receptor distribution in differentiating EG cells will be made. The binding and molecular characteristics of EGF-R in various cells will be compared to find out if different forms exist. Antibodies to EGF will be prepared and used to study the synthesis of EGF by mouse embryonic tissues and in teratocarcinoma cells by immunological methods. Endogenous growth factors produced by EC cells will be sought. We hope to establish embryonic cell lines using EGF and other factors to stimulate growth.

Identifying number: R01 CA 28531
Principal investigator: Karyl A. Rickard
Institution: Indiana University/Purdue University
Title: Nutrition Support of Children With Wilms' Tumor

Total FY79 obligation: N/A

Total FY80 obligation: $44,253
Nutrition allotment: 100%
Nutrition funding: $44,253

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The early diagnosis and multimodal treatment of children with Wilms' tumors have vastly improved survival rates. However, severe malnutrition (PEM) and numerous complications and toxicity are often associated with the treatment. Malnutrition reduces the capacity to withstand agressive treatment, increases susceptibility to opportunistic infections, depresses immune function and increases morbidity and mortality. The purpose of this study is to evaluate prospectively the benefits and complications of several modes of nutrition support (i.e., enteral nutrition, partial parenteral nutrition--PPN, peripheral nutrient infusion with enteral nutrition--and total parenteral nutrition--TPN, central nutrient infusion) in children (ages 1 to 7 years) receiving multimodal treatment for stages II-IV Wilms' tumors. Each regimen will be evaluated for its effectiveness in preventing or reversing PEM, maintaining or restoring immune competence, and obviating treatment modifications and complications. Children with stage II-IV Wilms' tumors who are considered malnourished at diagnosis will be randomized to receive either TPN or PPN throughout the period of irradiation. Nourished children with either stage IV or stages II/III and unfavorable histology Wilms' tumors will be randomized to receive either PPN or TPN throughout the 6 weeks of abdominal irradiation. Nourished children with stage II/III and favorable histology Wilms' tumors will receive either a comprehensive enteral nutrition program or PPN throughout the four weeks of intense treatment which includes abdominal irradiation. Thereafter, all children will receive a comprehensive enteral nutrition program to prevent subclinical PEM during 2, 3, or 4 drug chemotherapy maintenance programs. Nutritional state, immunological capacity, treatment modifications, and complications will be evaluated at diagnosis, 4, 6, 19, and 26 weeks during the initial, intense, and maintenance periods.

Identifying number: R01 CA 28629
Principal investigator: Willard J. Visek
Institution: University of Illinois, Champaign-Urbanna
Title: Hormones, Dietary Fat and Mammary Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $68,957
Nutrition allotment: 100%
Nutrition funding: $68,957

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objective is to study the relationships of dietary fat level, source, and their interactions to endocrine function and 7, 12-dimethylbenzanthracene (DMBA) breast carcinogenesis in rats. Diets varying in fat level (15 percent or 40 percent of total calories) and source (corn oil or beef tallow) will be used in all studies. Minerals, vitamins, and fiber will be supplied at a constant ratio per kilocalorie of dietary energy. Feed intake will be recorded. The effects of dietary fat on mammary carcinogenesis in intact, ovariectomized and ovariectomized-estrogen-implanted rats will be examined. We will determine if dietary fat modifies mammary carcinogenesis, circulating prolactin, and pituitary prolactin concentrations in three strains of rats with varying sensitivities to DMBA. We will further characterize the effects of dietary fat on 1) the capacity of the pituitary to secrete prolactin, 2) the secretory and metabolic clearance rates of prolactin, and 3) the circulating forms of prolactin and their relative immuno-activities.

Identifying number: R01 CA 28638
Principal investigator: William C. Topp
Institution: Cold Spring Harbor Laboratory
Title: Altered Nutritional Requirements for Growth

Total FY79 obligation: N/A

Total FY80 obligation: $75,526
Nutrition allotment: 100%
Nutrition funding: $75,526

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

All cultured cells with rare exceptions require a growth medium of low molecular weight nutrients (DME or Ham's F12) to be supplemented with serum. The serum provides high molecular weight factors required for cellular attachment, survival, and proliferation. Although these factors differ for each line it is possible to identify these individual requirements.

Altered Nutritional Requirements for Growth (continued)

Cells which have become transformed or tumorigenic have altered responses to normal growth regulatory pathways. In the work outlined in this grant, we will characterize the nutritional requirements for proliferation of a cloned normal rat embryo fibroblast line. We will transform this line with SV40, a small DNA virus, and characterize the way in which the virus/cell interaction has altered the nutritional requirements of the line. We will determine the tumorigenicity of the transformants, attempt to correlate the alterations in nutritional requirements with the degree of tumorigenicity, and recharacterize the nutritional requirements of tumor-derived sublines.

Transformed cells differ broadly in their properties from normal cells in culture. However, investigators have found recently that many of these growth patterns result from altered responses to serum hormones. In defined media several tumor lines studied reverted to "normal" behavior. We will undertake to identify good correlates of tumorigenicity in defined media for our transformants.

Identifying number: R01 CA 28645
Principal investigator: Herbert H. Wotiz
Institution: Boston University
Title: Vitamin B_6 and Hormone Action in Uterine and Breast Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $103,116
Nutrition allotment: 100%
Nutrition funding: $103,116

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

The response of normal and malignant estrogen target tissues to estradiol is determine by the concentration and retention time of nuclear receptor-estrogen complexes (RE_2). Vitamin B_6 inhibits nuclear binding of RE_2 by interfering with the cytoplasmic activation and nuclear retention reactions in vitro. It is the purpose of this study to further characterize these reactions and to determine if similar events can be observed in vivo using normal rat uterus and DMBA-induced mammary tumors. Furthermore, in vitro physicochemical analysis of estrogen receptor and anti-estrogen receptor states in the cytoplasm and nuclear cell fractions will be carried out in the presence and absence of specific chemical probes.

Identifying number: R01 CA 28677
Principal investigator: Peter S. Coleman
Institution: New York University
Title: Transport in Cholesterol-Rich Tumor Mitochondria

Total FY79 obligation: N/A

Total FY80 obligation: $79,640
Nutrition allotment: 100%
Nutrition funding: $79,640

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

Objective: To assess the effects of membrane cholesterol on the kinetics of citrate and adenine nucleotide transport across the inner mitochondrial membrane of two lines of Morris hepatomas and with normal mitochondria that have been exogenously enriched with cholesterol in vitro.

Approach: Mitochondria are isolated from Morris hepatomas 3924A and 16, from host livers, and from normal livers of ACI and Buffalo strain rats. Transport of citrate, malate, ATP and ADP is assessed according to both published procedures and via methods applicable specifically to this project. Mitochondria from normal livers will be isolated and enriched with cholesterol via a new "solid-state" molecule transfer methodology develped in this lab. We ask whether the enrichment of mitochondrial membranes with cholesterol, whether during tumor proliferation in the host or via solid-state transfer in vitro, is a sufficient membrane alteration to induce patterns of metabolic behavior that have been observed in mitochondria from a variety of tumors. The underlying rationale for this research is based on observation that the deregulation and enhanced rate of cholesterol biosynthesis appear to be two of the earliest metabolic alterations noted in virtually every hepatoma examined, and in a large number of other neoplastic cell types as well.

Identifying number: R01 CA 28725
Principal investigator: Sheldon M. Schuster
Institution: University of Nebraska
Title: Asparagine Biosynthesis in Normal and Tumor Cells

Total FY79 obligation: N/A

Total FY80 obligation: $66,744
Nutrition allotment: 10%
Nutrition funding: $6,674

Asparagine Biosynthesis in Normal and Tumor Cells (continued)

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

Some tumor cells have a nearly absolute requirement for exogenously supplied asparagine, while others can fulfill their requirements by endogenous biosynthesis. For this reason the enzyme responsible for the breakdown of asparagine has been used as a chemotherapeutic agent. The administration of inhibitors of the asparagine biosynthesis mechanism has also met with some therapeutic success. To enhance the effectiveness of selective tumor cell destruction, a complete understanding of asparagine biosynthesis is necessary. Much in fact remains unknown concerning the biosynthesis of asparagine. This ranges from determining the factors that control the asparagine synthesis rate in vivo to describing the metabolic needs for asparagine.

We have recently shown that asparagine synthetase from both pancreas and liver can exist in three molecular forms; a 113,000 alpha-form, a 57,000 beta-form and a 26,000 gamma-form. A dietary deficiency in asparagine results in the hepatic asparagine synthetase being in the alpha- and the beta-forms. When animals are given dietary asparagine, only beta-asparagine synthetase is found. Treatment of animals with asparaginase also results in the appearance of the alpha-form of asparagine synthetase. We have shown that the crude beta-form can be converted to the alpha-form by incubation with glutamine and magnesium. We propose to examine the three different forms of asparagine synthetase and to establish their role in the control of asparagine metabolism in both normal and tumor cells.

We have begun to explore the possible metabolic roles of asparagine in normal and tumor cell metabolism. We have found an enzyme in liver that can produce glyoxylate from isocitrate, and also another enzyme that uses asparagine and glyoxylate to form glycine. Possible links between asparagine and glycine metabolism are being investigated. Finding such a metabolic link may explain the selective cytotoxic effect exploited by asparaginase chemotherapy. It is hoped that these studies will uncover new targets for a rational approach to tumor chemotherapy.

Identifying number: R01 CA 28798
Principal investigator: Lester A. Reinke
Institution: University of North Carolina, Chapel Hill
Title: Influence of Ethanol on Carcinogen Activation

Total FY79 obligation: $65,808
Nutrition allotment: 100%
Nutrition funding: $65,808

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The research outlined in this proposal will examine interactions occurring between ethanol and the metabolic activation of chemical carcinogens. Isolated perfused rat livers will be used for these experiments, because the activation, conjugation, and binding of carcinogens to DNA may be studied simultaneously under physiological conditions. This research will be directed at three major objectives: 1) The influence of chronic ethanol administration on the metabolism of benzo(a)pyrene and dimethylnitrosamine in perfused livers and in isolated microsomes will be determined. In these experiments, the nutritional state will also be varied, in order to establish rate-limiting steps for carcinogen activation in whole cells. 2) The influence of the acute addition of ethanol on carcinogen activation will be studied. Direct effects of ethanol on enzymes of mixed-function oxidation and conjugation will be differentiated from indirect effects caused by the metabolism of ethanol and subsequent interactions with other metabolic pathways involved in carcinogen metabolism. 3) The effects of the acute and chronic addition of carcinogens on ethanol metabolism will be assessed by examining enzyme activity as well as the rate of reoxidation of NADH. Potential points of interactions will be determined and the mechanisms involved will be defined.

The increased risk of cancer (e.g., of the esophagus, colon, liver) in heavy consumers of ethanol is recognized as a significant health problem. The study of carcinogen activation in intact organs, coupled with measurement of metabolic intermediates and sophisticated optical techniques, such as surface fluorescence of pyridine nucleotides, comprise a unique approach to the study of ethanol-carcinogen interactions. These studies will for the first time define molecular mechanisms by which ethanol may increase the risk of cancer from chemical carcinogens.

Identifying number: R01 CA 28817
Principal investigator: Dennis R. Burholt
Institution: Allegeheny-Singer Research Corporation
Title: Dietary Aspects of Intestinal Response to Therapy

Total FY79 obligation: N/A

Total FY80 obligation: $53,687
Nutrition allotment: 100%
Nutrition funding: $53,687

Cancer activity/thrust: Nutrition/Treatment Research

Dietary Aspects of Intestinal Response to Therapy (continued)

Project description:

This preclinical research program is designed to:

1. Define the severity and time course of treatment (chemotherapy and/or radiotherapy) induced changes in animal weight, food and water intake, and gastrointestinal transit time.

2. Assess the extent to which the above factors contribute to the severity of acute gastrointestinal tissue toxicity (mainly, the proliferative response of the mucosa).

3. Attempt to ameliorate treatment-associated gastrointestinal toxicity through nutritional modifications, such as treatment dose-time scheduling, and enteral nutrient administration.

4. Assess the effect of pretreatment nutritional status on the proliferative response of the gastrointestinal epithelium to therapy.

Identifying number: R01 CA 29583
Principal investigator: Adelbert E. Wade
Institution: University of Georgia
Title: Effect of Dietary Fats on Chemical Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $38,894
Nutrition allotment: 100%
Nutrition funding: $38,894

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

That dietary fats alter susceptibility to chemically induced cancer has been demonstrated through epidemiological studies of human populations and experimental studies of laboratory animals. The mechanism by which responses to chemical carcinogens are altered is unknown. However, reasonable assumptions are that diet induces changes which increase or decrease tissue reactivity to carcinogen, or that diet influences activity of the mixed function oxidases which are responsible for the metabolic activation or detoxification of carcinogen. The objectives of this research are to determine the influences of the type of dietary fat on the activity of the mixed function oxidases of rat liver as these oxidases participate in the metabolic activation and/or detoxification of the potential carcinogens 3,4 benzo(a)pyrene 2-acetylaminofluorene and dimethylnitrosamine. Using hepatic microsomes from control and carcinogen-pretreated rats fed the specified saturated or unsaturated fats for 1 to 6 weeks, the in vitro metabolism of each carcinogen will be assessed. The apparent kinetics for the formation of each metabolite will be individually calculated. Correlation of metabolite and kinetic data with alterations in mutagenicity to appropriate strains of Salmonella using the reverse mutation system of Ames will indicate the significance of changes induced by dietary fats in chemical carcinogenesis. Correlation of metabolite and kinetic data with concentration and activity of components of the mixed function oxidase system will identify underlying physiologic processes altered by dietary fats.

Identifying number: R01 CA 30137
Principal investigator: Lester A. Reinke
Institution: University of Oklahoma Health Sciences Center
Title: Influence of Ethanol on Carcinogen Activation

Total FY79 obligation: N/A

Total FY80 obligation: $43,390
Nutrition allotment: 100%
Nutrition funding: $43,390

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The research outlined in this proposal will examine interactions occurring between ethanol and the metabolic activation of chemical carcinogens. Isolated perfused rat livers will be used for these experiments, because the activation, conjugation, and binding of carcinogens to DNA may be studied simultaneously under physiological conditions. This research will be directed at three major objectives: 1) The influence of chronic ethanol administration on the metabolism of benzo(a)pyrene and dimethylnitrosamine in perfused livers and in isolated microsomes will be determined. In these experiments, the nutritional state will also be varied, in order to establish rate-limiting steps for carcinogen activation in whole cells. 2) The influence of the acute addition of ethanol on carcinogen activation will be studied. Direct effects of ethanol on enzymes of mixed-function oxidation and conjugation will be differentiated from indirect effects caused by the metabolism of ethanol and subsequent interactions with other metabolic pathways involved in carcinogen metabolism. 3) The effects of the acute and chronic addition of carcinogens on ethanol metabolism will be assessed

Influence of Ethanol on Carcinogen Activation (continued)

by examining enzyme activity as well as the rate of reoxidation of NADH. Potential points of interactions will be determined and the mechanisms involved will be defined.

The increased risk of cancer (e.g., of the esophagus, colon, liver) in heavy consumers of ethanol is recognized as a significant health problem. The study of carcinogen activation in intact organs, coupled with measurement of metabolic intermediates and sophisticated optical techniques, such as surface fluorescence of pyridine nucleotides, comprise a unique approach to the study of ethanol-carcinogen interactions. These studies will for the first time define molecular mechanisms by which ethanol may increase the risk of cancer from chemical carcinogens.

Identifying number: R10 CA 13612
Principal investigator: Stephen Jones
Institution: University of Arizona, Tucson
Title: Southwest Oncology Group

Total FY79 obligation: N/A

Total FY80 obligation: $93,000
Nutrition allotment: 10%
Nutrition funding: $9,300

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

Clinical cancer treatment research to study the effectiveness of drugs, radiation therapy and immunologic agents. One subproject will include the use of metabolic diets in conjunction with a clinical trial of laetrile.

Identifying number: R10 CA 13630
Principal investigator: Leo Lagasse
Institution: University of California, Los Angeles
Title: Gynecologic Oncology Group

Total FY79 obligation: [illegible]

Total FY80 obligation: $92,000
Nutrition allotment: 10%
Nutrition funding: $9,200

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

The institution will register (with the group statistical office) all new gynecologic cancer patients seen at participating hospitals (number of cases annually approximately 300). We predict that 64 patients will be enrolled on protocols in the coming year.

One subproject of this study will include the use of metabolic diets in conjunction with a clinical trial of laetrile.

Identifying number: R10 CA 13650
Principal investigator: Richard Hahn
Institution: Mayo Foundation, Rochester, NY
Title: Eastern Cooperative Oncology Group

Total FY79 obligation: N/A

Total FY80 obligation: $223,000
Nutrition allotment: 10%
Nutrition funding: $22,300

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

The specific objective of this project is to participate in group activities aimed at improving the total care of cancer patients. This would include efforts to improve diagnostic procedures and therapy, particularly clinical pharmacologic studies on new cancer chemotherapeutic agents. Although emphasis would be placed on direct patient care, primarily conducted on an outpatient basis, we would also hope to participate in group activities pertinent to immunologic studies, epidemiologic studies, and natural history and biologic patterns of specific neoplasms.

One subproject of this study will include the use of metabolic diets in conjunction with a clinical trial of laetrile.

Identifying number: R10 CA 23742
Principal investigator: Denis Miller
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Children's Cancer Study Group

Total FY79 obligation: N/A

Total FY80 obligation: $79,000
Nutrition allotment: 10%
Nutrition funding: $7,900

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

The Children's Cancer Study Group is a national cooperative group of institutions comprised of multidisciplinary groups of pediatric oncologists, hematologists, radiotherapists, surgeons, immunologists, pathologists and biostatisticians and dedicated to the objective of improving the prognosis and survival of children with leukemia, lymphomas and solid malignant tumors through controlled, clinical trials employing multimodal therapy. In addition to large scale phase III studies in leukemia and other cancers, the group has active phase II protocols utilizing newer investigational drugs. Natural history of disease, immunotherapy, special studies related to disease and treatment complications, and dissemination of newly acquired knowledge on cancer diagnosis and treatment to the medical community at large are other objectives of the group.

Currently, patients with the following diseases are being entered on group protocols: ALL (CCG 161162-163), non-Hodgkin's lymphoma (CCG 541), medulloblastoma (CCG 941), high-grade astrocytoma (CCG 943), brain stem glioma (CCG 944), Wilms' tumor II (CCG 441), retinoblastoma, rhabdomyosarcoma, neuroblastoma, Ewing's sarcoma, hepatoma gonadal. and germ cell tumors, histiocytosis and ostenogenic sarcoma. Special studies relating to infectious disease complications and natural history are under investigation.

One subproject of this study will include the use of metabolic diets in conjunction with a clinical trial of laetrile.

Identifying number: R13 CA 27543
Principal investigator: Donald L. Morton
Institution: University of California, Los Angeles
Title: Surgical Oncology Research Planning Workshop

Total FY79 obligation: $34,990
Nutrition allotment: 12%
Nutrition funding: $4,199

Total FY80 obligation: Active, not funded
Nutrition allotment: 12%
Nutrition funding: None

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Project description:

A Surgical Oncology Research Planning Workshop is planned for November 1979. The objectives of this workshop are as follows: 1) review and assess the state of science in surgical oncology; 2) develop a scientific plan and recommendations for future research activities in surgical oncology; 3) develop plans for fostering collaborative research among investigators in surgical oncology and their colleagues in other areas of cancer research; 4) assess the resources required for future research in surgical oncology and make recommendations regarding priorities for the allocation of available resources; and 5) prepare a research plan and report for submission to the Board of Scientific Counselors of the Division of Cancer Treatment of the National Cancer Institute and the Board of Directors of the American Cancer Society regarding these activities.

Identifying number: R13 CA 27751
Principal investigator: Brian E. Henderson
Institution: University of Southern California
Title: Epidemiology and Cancer Registries in the Pacific Basin

Total FY79 obligation: N/A

Total FY80 obligation: $77,374
Nutrition allotment: 50%
Nutrition funding: $38,687

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This proposal requests funds for travel and per diem for 50 participants to the Third Symposium on Epidemiology and Cancer Registries in the Pacific Basin. The first and second symposia (1975 and 1978) provided a forum for the exchange of information on 1) the design and conduct of cancer registries, and 2) the status of research in cancer epidemiology in nineteen participating countries and territories of the Pacific. In addition, important collaborative research on several cancers (e.g., lung, breast, nasopharynx and liver) was developed.

The third symposium will be designed to provide new demographic information from existing cancer registries (e.g., secular trends, occupational risk) and to introduce data from developing registries in the

Epidemiology and Cancer Registries in the Pacific Basin (continued)

People's Republic of China, Korea, and the South Pacific. In addition, ongoing collaborative research will be reviewed and new projects designed during workshops on cancer sites of particular interest-liver, breast, stomach, colorectal, lung, urinary bladder, and prostate and testis. One of the major topics of interest will be the current research in the area of diet and breast cancer risk. Dr. Henderson will visit several of the participating programs prior to the third symposium to provide added stimulus to the meeting preparations.

Identifying number: R18 CA 16405
Principal investigator: Robert O. Johnson
Institution: University of Wisconsin, Madison
Title: Regional Cancer Control Program

Total FY79 obligation: $529,684
Nutrition allotment: 5%
Nutrition funding: $26,484

Total FY80 obligation: $570,837
Nutrition allotment: 5%
Nutrition funding: $28,542

Cancer activity/thrust: Cancer Control

Project description:

This program includes cooperative projects in cancer prevention, treatment, and rehabilitation, including nutritional aspects of these interventions.

Identifying number: R18 CA 17867
Principal investigator: Charles Arnold
Institution: American Health Foundation
Title: Cancer Control and Prevention Program Support

Total FY79 obligation: $82,801
Nutrition allotment: 60%
Nutrition funding: $49,681

Total FY80 obligation: Active, not funded
Nutrition allotment: 60%
Nutrition funding: None

Cancer activity/thrust: Cancer Control

Project description:

The purpose of this program is to investigate the effectiveness of cancer detection, comparing a full screening procedure with detection through a much simpler prescreen reaching a larger population in their work setting. It includes application of motivational programs to areas of proper nutritional habits among school children and adults.

Identifying number: R18 CA 17868
Principal investigator: Jerome W. Yates
Institution: University of Vermont and State Agricultural College
Title: Cancer Care and Rehabilitation in a Rural Setting

Total FY79 obligation: Active, not funded
Nutrition allotment: 75%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Rehabilitation/Treatment Research

Project description:

Patients with advanced cancer are being monitored in their homes in an attempt to improve their quality of life. Evaluation data will continue to be collected on those patients currently entered in the study and new patients as they are entered. Evaluation and interpretation of the data collected thus far will be expanded and modified based on the findings. An evaluator-referee will join the project staff to stabilize interpretation of the study design and to insure consistency in interview technique. Particular attention will be given to correlation of electromyography and nerve conduction data and nutritional status. An ongoing reassessment will be made of changes in staff attitudes and values.

Identifying number: R18 CA 17928
Principal investigator: C. E. Butterworth, Jr.
Institution: University of Alabama, Birmingham
Title: Nutritional Support and Rehabilitation for Cancer Patients

Total FY79 obligation: $79,990
Nutrition allotment: 100%
Nutrition funding: $79,990

Nutritional Support and Rehabilitation for Cancer Patients (continued)

Total FY80 obligation: $93,509
Nutrition allotment: 100%
Nutrition funding: $93,509

Cancer activity/thrust: Cancer Control

Project description:

Evaluation of the effectiveness of aggressive nutrition therapy in support of existing methods of support for cancer patients will be continued. Preliminary experience has shown that parenteral and enteral feeding programs extend tolerance for chemotherapy and enhance the quality of life. During the coming year, data will be gathered concerning the status of eight vitamins by automated screening methods. This information should facilitate early diagnosis and management of vitamin problems, in addition to diagnostic and therapeutic methods currently in use.

Identifying number: R18 CA 18871
Principal investigator: James E. Potchen
Institution: Michigan State University
Title: A Community-Based Study of Colorectal Cancer Control

Total FY79 obligation: Active, not funded
Nutrition allotment: 6%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Cancer Control

Project description:

The purpose of this project is to identify clinical, radiologic, and behavioral patterns in the use of radiologic diagnostic procedures for the detection of colorectal cancer. In the forthcoming year, this research will concentrate in four primary areas. 1) Extensive analysis will be done on signs and symptoms and diagnostic data collected on 3,000 barium enema examinations administered over 4 months in community hospitals across the mid-Michigan area. Standard frequency methods as well as pattern-detection techniques will be used to identify groups of patients at risk for colon cancer and to increase the yield of positive examination. 2) Investigation will continue of physician behavior in ordering the barium enema examination, with the hopes of developing an algorithm for optimal use of the exam. 3) Further investigation will be made of factors influencing false-negative examinations and the establishment of an information system combining the results with selected cancer registry data for use by community hospitals across Michigan. 4) It is planned to provide cost estimates computation and definition of optimal economic use of radiologic diagnostic procedures.

The information obtained from these studies will be used to recommend additional guidelines for the control and management of colorectal cancer.

Identifying number: R18 CA 18901
Principal investigator: Jerilyn A. Logemann
Institution: Northwestern University
Title: Evaluation of Rehabilitation of Oropharyngeal Cancer

Total FY79 obligation: $77,357
Nutrition allotment: 10%
Nutrition funding: $7,736

Total FY80 obligation: $64,361
Nutrition allotment: 100%
Nutrition funding: $64,361

Cancer activity/thrust: Rehabilitation/Treatment Research

Project description:

This study is designed to evaluate the effects of ablation surgery of the oral cavity and oropharynx and associated reconstructive and nutritional rehabilitation of patients.

Identifying number: R18 CA 19378
Principal investigator: William Regelson
Institution: Virginia Commonwealth University
Title: Supportive Programs for Cancer Patients

Total FY79 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Rehabilitation/Treatment Research

Project description:

The objective of this study is to determine the efficacy of psychoactive agents, analgesics, antiemetics, hypnotics, and appetite stimulants in cancer patients. Butorphenol has been found to be an effective analgesic in postoperative patients. Delta 9-THC is an effective antianxiety agent. Preliminary study confirms lithium carbonate's granulocyte-stimulating activity, but patient accrual is limited by contraindications. Studies on supplementation with 19-OH testosterone, domperidone, and zinc do not warrant further study as mood modifiers, antiemetics, and appetite stimulants. Nabilone is a priority drug to be studied next for action as a potential antiemetic, antianxiety, and appetite-stimulating agent.

Psychometric testing establishes the usefulness of reassurance in clinical treatment. Studies of visual imagery, music, and supportive environments (kinesthetic room) are under way.

Identifying number: R18 CA 19632
Principal investigator: Thomas F. Nealon, Jr.
Institution: St. Vincent's Hospital and Medical Center,
New York
Title: Nutritional Component of Cancer Therapy

Total: FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None
Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Nutrition/Treatment Research

Project description:

The deficiency in nutrition of cancer patients which is present throughout the course of the disease frequently complicates and negates attempts at proper therapy. The contribution of specifically formulated chemical diets as an adjunct to cancer chemotherapy will be studied by delineating the causes of the malnutrition, quantitating the influence of the nutritional status on the efficacy of chemotherapy, and quantitating the effect of the special diets on serum albumin, blood count, blood chemistries, and plasma amino acid levels. These values will be correlated with nutritional intake, histologic diagnoses, status of disease, and response to chemotherapy. Patients with liver metastases will be maintained nutritionally with specially formulated chemical diets in an attempt to enhance their response and tolerance of cancer chemotherapy.

Identifying number: R18 CA 20876
Principal investigator: Jerilyn A. Logemann
Institution: Northwestern University
Title: Prosthetic Rehabilitation of Oropharyngeal Cancer

Total FY79 obligation: $63,890
Nutrition allotment: 15%
Nutrition funding: $9,583

Total FY80 obligation: Active, not funded
Nutrition allotment: 15%
Nutrition funding: None

Cancer activity/thrust: Rehabilitation/Treatment Research

Project description:

This project is to evaluate the effects of intraoral prostheses on the communication and nutritional rehabilitation of patients after ablative surgery for oropharyngeal cancer.

Identifying number: R18 CA 22091
Principal investigator: Condict Moore
Institution: University of Louisville
Title: Cancer Control Developmental and Support Grant

Total FY79 obligation: $317,359
Nutrition allotment: 15%
Nutrition funding: $47,604

Total FY80 obligation: $347,650
Nutrition allotment: 15%
Nutrition funding: $52,148

Cancer activity/thrust: Cancer Control

Project description:

One of the activities forming a part of this program is nutritional management, which has as its purpose the development of a clinical service demonstration of the dietary and nutritional management of cancer patients.

Identifying number: R18 CA 25521
Principal investigator: Charles Arnold
Institution: American Health Foundation
Title: Primary Prevention of Cancer in Childhood

Total FY79 obligation: N/A

Total FY80 obligation: $407,204
Nutrition allotment: 25%
Nutrition funding: $101,801

Cancer activity/thrust: Cancer Control

Project description:

Nine hundred students, initially ages 9 and 10 years, will take part in a controlled clinical trial in which the major objective, will be:

(1) to identify major cancer and other disease risk factors;

(2) to reduce elevated risk status through planned intervention actvities; and

(3) to reinforce and maintain reduced risk status.

The major outcome sought will be the primary prevention of cigarette smoking through a peer group approach. In addition, nutrition activities will seek to improve nutritional habits and decrease clinical indices of overnutrition. Four program components will provide a motivational sequence of events favoring health-related behavior change. These components are (a) screening, (b) return of screening results to child, (c) curriculum education materials, and (d) antismoking and other interventions. Evaluation will be done by comparing smoking onset rates in study versus control schools. In addition, overall risk index scores will be compared as determined from annual rescreening and questionnaires.

Identifying number: R18 CA 26619
Principal investigator: Jane Dixon
Institution: Yale University
Title: Nursing Interventions in Nutrition of Cancer Patients

Total FY79 obligation: $176,860
Nutrition allotment: 100%
Nutrition funding: $176,860

Total FY80 obligation: $150,452
Nutrition allotment: 100%
Nutrition funding: $150,452

Cancer activity/thrust: Cancer Control

Project description:

Persons with cancer often develop nutritional complications as a result of their disease or its treatment, and, in turn, nutritional deficiencies are known to diminish an individual's ability to tolerate therapies and to recover from the disease. Little is known concerning methods through which the quantity and quality of oral intake of the cancer patient can be augmented by the health professional.

The major objective of this project is to conduct a clinical nursing experiment designed to evaluate the effectiveness of three specific nursing intervention protocols and a control nursing condition on the food-intake patterns, nutritional status, and performance status of cancer patients. These intervention protocols will involve emphasis on frequent nutritional supplements, preprandial relaxation techniques, and preprandial oral hygiene techniques. Subjects will be monitored for 18 months. The anticipated result of this project will be a preliminary system for assessing the malnourished or potentially malnourished cancer patient and prescribing subsequent nutritional intervention. Such a system may enable nurses to improve the nutritional well-being of cancer patients, thus enhancing their response to therapy and the quality of their lives.

Identifying number: R18 CA 27683
Principal investigator: Vincent P. Vinciguerra
Institution: North Shore University Hospital, Manhasset, N.Y.
Title: Improved Cancer Care Through a Home Program

Total FY79 obligation: N/A

Total FY80 obligation: $107,660
Nutrition allotment: 15%
Nutrition funding: $16,149

Cancer activity/thrust: Cancer Control

Project description:

The optimal pattern of cancer care for patients failing standard therapy remains unsettled. Three paths are now available in the United States for terminal care: 1) hospitalization, 2) hospice or chronic care institutionalization, or 3) home care.

Improved Cancer Care Through a Home Program (continued)

This study is designed to evaluate the choice of hospitalization vs. home care with optimal medical support to determine whether:

1. Home care is cost-effective.
2. Psychologic adjustment to the illness by both family and patient are modified by pattern of care.
3. Survival and quality of life is enhanced by home care.
4. Narcotic usage is modified by environment.

Patients with evidence of progressive cancer in spite of optimal medical therapy will be studied prospectively by a physician, social worker, and dietician to determine whether or not home care is beneficial. Standard techniques such as the Karnofsky Index, profile of mood states, multiple affect adjective check list and caloric count will be applied to equivalent groups of patients who receive medical support either in the hospital or at home.

Identifying number: R18 CA 28005
Principal investigator: Robert L. Baehner
Institution: Indiana University/Purdue University
Title: Prevention/Reversal of Malnutrition in Neuroblastoma

Total FY79 obligation: N/A

Total FY80 obligation: $57,240
Nutrition allotment: 100%
Nutrition funding: $57,240

Cancer activity/thrust: Rehabilitation/Treatment Research

Project description:

The prognosis for stage IV children with neuroblastoma is dismal. Aggressive multimodal treatment programs often result in severe malnutrition (PEM) which interferes with therapy and increases morbidity and mortality. The plan of this study is to evaluate the effectiveness of enteral and parenteral nutrition in preventing and/or reversing PEM, maintaining or restoring immune competence, preventing treatment delays, and improving tumor response of 36 children (ages 1 to 6 years) with metastatic neuroblastoma receiving chemotherapy (five drugs: cytoxan, vincristine, DTIC, adriamycin, VM-26) every 3 weeks. Children who are considered nourished at diagnosis will be randomized to receive either a comprehensive enteral nutrition program or total parenteral nutrition (TPN) for the first 35 days of treatment. Children considered malnourished at diagnosis will be randomized to receive either TPN or partial parenteral nutrition plus enteral nutrition for the first 35 days of the treatment. Thereafter, all children will receive a comprehensive enteral nutrition program. Nutritional status, recall skin test response, treatment delays, and tumor response will be evaluated at 0, 6, 12, 18, and 22 weeks. Additional nutritional evaluations (dietary, anthropometric, and biochemical) will be determined weekly during the first 5 weeks to identify nutritional indices of clinical and subclinical PEM in children undergoing treatment for metastatic neuroblastoma.

Identifying number: R18 CA 28072
Principal investigator: Jerome J. De Cosse
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Nutritional Rehabilitation in Head and Neck Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $227,012
Nutrition allotment: 100%
Nutrition funding: $227,012

Cancer activity/thrust: Rehabilitation/Treatment Research

Project description:

The objective of the proposed randomized trial is to compare intensive nasogastric tube feeding with optimal oral nutrition in patients with advanced head and neck cancer. The overall goal is to evaluate the effects of nutritional support on patients' ability to tolerate and respond to radiation therapy and chemotherapy, as well as its effects on recurrence and survival.

Among the questions to be studied are differences in protein and caloric intake; differences in weight; differences in amount and duration of therapy; severity of mucositis, skin reactions, and taste and smell impairment during therapy; the pattern of recovery of taste following therapy and the effects of zinc on the recovery; techniques for improving patient nutrition, both orally and extra-orally; and the long-term consequences of aggressive nutritional support during relatively short-term therapy.

Identifying number: R23 CA 25601
Principal investigator: Neil Sidell
Institution: University of California, Los Angeles
Title: Effects of Retinoic Acid on the Immune System

Total FY79 obligation: $32,750
Nutrition allotment: 100%
Nutrition funding: $32,750

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Immunology/Treatment Research

Project description:

Vitamin A and its derivatives (retinoids) exhibit potent antitumor activity. They are capable of retarding the appearance or reducing the incidence of tumors induced by chemical carcinogenesis or virus, and they inhibit the growth of several transplantable tumors. These effects have been proposed to be at least partially due to stimulatory effects on the immune system.

The objective of this study is to analyze in detail the effects of one retinoid (retinoic acid) on the immune system. The effects of retinoic acid (RA) on the in vivo and in vitro humoral response of various cell types will be explored. The effects of this compound on the various effector arms of the cell-mediated immune response will also be studied. The response of mice to allogeneic tumor cells will be used to evaluate the effects on killer cells and macrophages, and the response to xenogeneic erythrocytes will be used to assay for antibody-dependent, cell-mediated lysis, and the delayed type of hypersensitivity reaction.

This study will thus provide valuable information for the proper use of RA in clinical applications of immune regulation and as a modality of treatment against neoplasia.

Identifying number: R25 CA 17982
Principal investigator: Bernard Gardner
Institution: Downstate Medical Center
Title: Clinical Cancer Education Program

Total FY79 obligation: N/A

Total FY80 obligation: $107,877
Nutrition allotment: 3%
Nutrition funding: $3,236

Project description:

This cancer education grant is designed to supplement the usual cancer education offered in the medical school curriculum with a series of electives servicing 60-80 medical students per year. An expanded program of conferences, rounds, seminars, and special exercises run by faculty members; teaching associates will be offered to 440 third and fourth year students, 450 house staff and community physicians in 36 outlying hospitals in Brooklyn. Special programs in the epidemiology of cancer have been created in a special effort designed to bring epidemiology, carcinogenesis and data relative to nutrition in cancer development and treatment to the attention of our students and housestaff. A new evaluation program is described to test the effectiveness of our student oncology teaching programs.

Identifying number: R25 CA 17985
Principal investigator: Condict Moore
Institution: Universty of Louisville
Title: Clinical Cancer Education Program

Total FY79 obligation: $130,935
Nutrition allotment: 0.27%
Nutrition funding: $353

Total FY80 obligation: $132,176
Nutrition allotment: 0.27%
Nutrition funding: $357

Project description:

The general purpose of this program is to achieve the highest level of care in the cancer patient by ensuring that medical students, residents, fellows, nurses, and practitioners acquire and maintain a basic knowledge and understanding of cancer, including prevention, detection, treatment, and rehabilitation.

This work encompasses the following specific aims: 1) providing clinical cancer training experiences for 15 clinical assistants and 4 clinical associates; 2) providing high-quality continuing cancer education programs for the faculty and area health professionals through a formal oncology lecture series; 3) expanding the cancer educational outreach programs; 4) improving the coordination of the education program; 5) evaluating the core curriculum in the school of medicine as to its adequacy in light of these objectives; 6) developing and implementing a cancer computer-assisted self-evaluation program; 7) developing a nursing oncology program for undergraduates, master's degree candidates, Clinical Cancer Education Program (continued)

and practitioners; 8) developing better, practical mechanisms for evaluating cancer education programs; and 9) assisting the university hospital cancer committee, in the development of a manual for patient care.

Identifying number: R25 CA 17990
Principal investigator: Harold J. Wanebo
Institution: University of Virginia, Charlottesville
Title: Clinical Cancer Education Program

Total FY79 obligation: N/A

Total FY80 obligation: Active, not funded
Nutrition allotment: 3%
Nutrition funding: None

Project description:

The objective of the Clinical Cancer Education Program is to complete the development, implementation, and evaluation of an interdisciplinary cancer curriculum at the undergraduate, graduate, and continuing education levels. The program will be geared toward establishing an educational curriculum for the medical students, house staff, and clinical associates, as well as offering education opportunities for the University of Virginia staff, local physicians, and other allied health personnel.

The primary objective for the undergraduate curriculum is the development of a book of cancer objectives. This book will ensure that the student will have a defined body of required knowledge of cancer studies by the end of his 4 years.

The emphasis for the development of the graduate program will be to expand the Clinical Associate Program into a multidisciplinary program such that every clinical associate in any of the oncology specialties will have exposure to radiation therapy, chemotherapy, and surgery, the three major areas of treatment.

In the continuing education aspect of the program, proposed objectives are to develop a program specifically designed for those at the postgraduate level who desire updating and expansion of their cancer knowledge and to develop a program of cancer education for medical personnel other than physicians in the form of a multidisciplinary cancer studies elective.

Identifying number: R25 CA 17998
Principal investigator: Charles M. Huguley, Jr.
Institution: Emory University
Title: Clinical Cancer Education Program

Total FY79 obligation: $167,484
Nutrition allotment: 0.5%
Nutrition funding: $837

Total FY80 obligation: $126,486
Nutrition allotment: 0.5%
Nutrition funding: $632

Project description:

This project is to continue and expand the Clinical Cancer Education Program, specifically 1) to improve coordination through the Interdepartmental Clinical Cancer Education Committee of all cancer-related teaching during the basic science years to ensure an integrated core cancer curriculum for all students; 2) to expand interdisciplinary teaching during the clinical clerkship and housestaff years through improved tumor conferences and increasing interdisciplinary participation in the care of each cancer patient; 3) to increase the opportunity for specialized training in oncology for students (clinical assistants) and postresidency clinical associates by expanding internship programs and student electives in oncology and to provide a more formal structure of interdisciplinary teaching for student clinical assistants and students on electives and for the postresidency clinical associates; 4) to continue the development of teaching aids for self-study use at all levels; 5) to provide special lectureships in oncology by national authorities for all elements of the medical school and for practicing physicians, and 6) to operate an interdepartmental oncology ward at Grady Hospital for a demonstration center for improved cancer care to medical students, housestaff, postgraduate physicians, nurses, physician's associates and social workers.

Identifying number: R25 CA 18039
Principal investigator: John R. Hartmann
Institution: Children's Orthopedic Hospital-Medical Center
Title: Clinical Cancer Education Program (Pediatric)

Total FY79 obligation: N/A

Total FY80 obligation: $74,224
Nutrition allotment: 3%
Nutrition funding: $2,227

Clinical Cancer Education Program (Pediatric) (continued)

Project description:

The aim of this proposal is to continue to develop a model education program in pediatric oncology for teaching associates, housestaff, practicing physicians, medical students, nurses, social workers, and other paramedical disciplines. Established clinical and research programs of this comprehensive cancer center together with a formal teaching curriculum, conferences, and self-teaching audiovisual aids will be used. The program will be responsive to changing needs in pediatric oncology, with greater emphasis on epidemiology, pharmacology, and the need to develop pediatric oncologists with the ability to develop innovative clinical and laboratory reseach programs. Frequent and in-depth evaluation of the program will be performed.

Identifying number: R25 CA 26047
Principal investigator: Charles A. Coltman, Jr.
Institution: University of Texas, San Antonio
Title: Clinical Cancer Education Program

Total FY79 obligation: N/A:

Total FY80 obligation: $104,302
Nutrition allotment: 5%
Nutrition funding: $5,215

Project description:

An intensive review and documentation of the interdisciplinary oncology curriculum through the 4 years of medical school has been initiated. The product of this process will be a manual of oncology objectives and review questions. An oncology test is administered yearly to graduating seniors to measure their knowledge of oncology topics. The test items are cross-referenced with the oncology objectives. Analysis of students' performances on the oncology items from the NBME parts I and II is also done yearly as another measure of student achievement. Short audio tapes on various oncology topics are being developed and will be available to students and house staff via telephone. The tapes will address the proper procedures for the diagnosis and work up to oncology patients. Programs for clinical associates (fellows) and clinical assistants (students) have been implemented and are ongoing. Continuing education courses for physicians and community awareness programs for the public are done annually.

Identifying number: R25 CA 28248
Principal investigator: Darryl M. Williams
Institution: Louisiana State University Medical Center, Shreveport
Title: Clinical Cancer Education Program

Total FY79 obligation: N/A

Total FY80 obligation: $43,813
Nutrition allotment: 3%
Nutrition funding: $1,314

Project description:

Louisiana State University Medical Center in Shreveport is rapidly emerging as a cancer treatment and education resource for a large geographic area which previously had had no effective educational program or referral center. The purposes of this proposed cancer education program are: 1) to provide amplification of present educational program at all levels, including undergraduate, graduate, and postgraduate medical education; and 2) to develop new educational programs at all levels. Efforts will be made to develop an expanded educational program with the university so that students will be able to participate in patient care, clinical investigation, and/or cancer-related bench research. Clinical associates will learn about the needs and care of the individual patient as well as the role for cooperative studies. There will be emphasis on locally produced television and audiovisual aids as well as increased efforts to communicate with practicing physician's home communities. Assessment of effectiveness of these programs will be made by examination of student scores in standardized tests before and after institution of the program as well as with attitudinal surveys carried out among students, house officers, and practicing physicians.

Identifying number: R26 CA 14523
Principal investigator: A. M. Pamukcu
Institution: University of Wisconsin, Madison
Title: Urinary Bladder Carcinogenesis by Bracken Fern

Total FY79 obligation: $141,889
Nutrition allotment: 100%
Nutrition funding: $141,889

Total FY80 obligation: $109,610
Nutrition allotment: 100%
Nutrition funding: $109,610

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Urinary Bladder Carcinogenesis by Bracken Fern (continued)

Project description:

Cows, rats, and mice are highly susceptible to urinary bladder carcinogenesis by bracken fern. Milk obtained from cows ingesting bracken fern contains toxic, mutagenic, and carcinogenic metabolites not normally present in cow milk. Humans ingesting bracken fern or such milk might be unwittingly exposed to a naturally occurring plant carcinogen. Human consumption of this plant predisposes to an augmented risk to esophageal carcinoma. Tannin isolated from bracken fern is noncarcinogenic when given orally, but was tumorigenic when administered subcutaneously or implanted intravesically. Carcinogenicity of bracken fern appears not to be associated with tannin when given orally, because tannin-free fractions of bracken fern are carcinogenic when fed to rats. The urine of rats given tannin-free fraction of bracken fern contains mutagenic metabolites not present in urine of rats fed tannin. Carcinogenic compound(s) in tannin-free fractions of bracken fern and carcinogenic metabolites in milk from bracken-fed cows will be identified and tested for carcinogenic activity with the use of rodents and microbiological systems.

Identifying number: R26 CA 15638
Principal investigator: Lee W. Wattenberg
Institution: University of Minnesota
Title: Inhibition of Neoplasia of the Large Bowel

Total FY79 obligation: $106,919
Nutrition allotment: 100%
Nutrition funding: $106,919

Total FY80 obligation: $114,236
Nutrition allotment: 100%
Nutrition funding: $114,236

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This investigator is studying methods of prevention of chemical carcinogen-induced neoplasia of the large bowel. He is investigating the effects of antioxidants on the effects of chemical carcinogens. One type of antioxidant being studied includes those which are not absorbed in the gastrointestinal tract and a second group of antioxidants includes those which are absorbed in the gastrointestinal tract. These studies are aimed at determining the mechanism of inhibition and the conditions under which such inhibition occurs.

Identifying number: R26 CA 15957
Principal investigator: Morris Pollard
Institution: University of Notre Dame
Title: Intestinal Carcinogenesis in Conventional and Germfree Rats

Total FY79 obligation: $71,472
Nutrition allotment: 10%
Nutrition funding: $7,147

Total FY80 obligation: $82,466
Nutrition allotment: 10%
Nutrition funding: $8,247

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The objective of this project is to examine environmental and endogenous factors that contribute to the development of intestinal cancer. This involves determinations of etiological agents by a standard protocol and the levels of susceptibilities manifested by several strains of laboratory rats in response to such treatments. This protocol will be used to assay prophylactic and therapeutic procedures that relate to the disease in humans, including cytotoxic and immunopotentiating drugs, radiation, and radiation-induced bone marrow chimerism, and a new antitumor lipoprotein recovered from sera of pregnant rats.

Identifying number: R26 CA 16375
Principal investigator: William H. Elliott
Institution: St. Louis University
Title: Role of Bile Acids in Etiology of Large Bowel Cancer

Total FY79 obligation: $75,600
Nutrition allotment: 100%
Nutrition funding: $75,600

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The objective of this study is to define the relationship of bile acids or their metabolites with the etiology of cancer of the large bowel. This project will continue an investigation of the effects of diet on the quantity and nature of bile acids in the enterohepatic circulation of the

Role of Bile Acids in Etiology of Large Bowel Cancer (continued)

rat by analyses of small aliquots of rat bile obtained at regular intervals. Identification and quantitation of bile acids will be done by recently improved methods involving enzymatic assay, high-pressure liquid chromatography, glass capillary-gas chromatography, and glass capillary gas chromatography-mass spectrometry coupled with an on-line computer.

Identifying number: R26 CA 16382
Principal investigator: Bandaru S. Reddy
Institution: American Health Foundation
Title: Metabolic Epidemiology of Colon Cancer

Total FY79 obligation: $103,919
Nutrition allotment: 100%
Nutrition funding: $103,919

Total FY80 obligation: $95,722
Nutrition allotment: 100%
Nutrition funding: $95,722

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The overall objectives of this research are to 1) acquire significant information on the mechanisms related to, and the role played by dietary components, intestinal microflora, and their metabolites on the etiology of colon cancer in humans; 2) identify specific environmental and dietary components that either directly cause colon cancer or indirectly promote the formation and development of colon neoplasms; and 3) develop key biochemical and/or microbial indicators which distinguish low-risk and high-risk populations for colon cancer.

The study will determine the fecal cholesterol and bile acid metabolites and fecal bacterial 7-alpha-dehydroxylase, cholesterol dehydrogenase, and nuclear dehydrogenase activities and fecal bacterial transnitrosation reaction in members of high-risk cancer families, patients with familial polyposis, and healthy controls consuming a mixed-Western diet. The study determining the metabolic activity of fecal microflora (above enzyme parameters) in patients with colon cancer and adenomatous polyps to permit an evaluation of these discriminants for colon cancer will be continued. In addition, it is planned to isolate and identify the mutagens (presumptive carcinogens) in the feces of these study populations.

Identifying number: R26 CA 16750
Principal investigator: Selwyn A. Broitman
Institution: Boston University
Title: Diet, Flora, and Colon Tumorigenesis

Total FY79 obligation: $99,342
Nutrition allotment: 100%
Nutrition funding: $99,342

Total FY80 obligation: $98,133
Nutrition allotment: 100%
Nutrition funding: $98,133

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The long-term objective of this project is to identify nutritional factors that contribute to the high incidence of colon cancer in Western culture. Studies will focus on the role of dietary and endogenous cholesterol and its metabolites in the gut lumen in large bowel tumorigenesis in an experimental animal. Continuing studies are planned on the interrelationship between dietary polyunsaturated fat and saturated fat, particularly as it relates to the disbursement of cholesterol systemically and/or enterally. Various nutritional regimens containing 20 percent fat with and without cholesterol are fed to rats given an indirect acting carcinogen, 1, 2-dimethylhydrazine (subcutaneously or orally), or a direct acting carcinogen, *N*-methyl-*N*-nitro-*N*-nitroguanidine (intrarectally).

These diets will allow an evaluation of the interrelationships among the quality of dietary fat, the enteral excretion of cholesterol and its metabolites, and large bowel tumorigenesis. Effects of cholesterol and its metabolites will be evaluated in terms of tumor number, histological type and location, latency period, and tumor incidence. An assessment of fecal excretion of neutral and acid sterols as well as fecal 7-alpha-dehydroxylase and cholesterol dehydrogenase activities occurring in rats fed the various dietary regimes will permit correlative studies with large bowel tumorigenesis. With the use of the Ames Salmonella/microsomal assay for mutagens/carcinogens, various fecal sterol metabolites will be evaluated to pinpoint those components which may be carcinogenic or cocarcinogenic for further testing.

These studies should provide 1) a better understanding of the relationships among nutrition, microflora, and colonic cancer; 2) additional information concerning the nutritional linkage between coronary heart disease and colon cancer; and 3) additional guidelines for studies in human nutrition aimed at decreasing the incidence of colon cancer.

Identifying number: R26 CA 16908
Principal investigator: Frederick R. De Rubertis
Institution: Veterans Administration Hospital
Title: Cyclic Nucleotides in Colonic Carcinogenesis

Total FY79 obligation: $44,142
Nutrition allotment: 15%
Nutrition funding: $6,621

Total FY80 obligation: $46,513
Nutrition allotment: 15%
Nutrition funding: $6,977

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Large bowel cancer in humans is probably induced by carcinogens and cocarcinogens present in the bowel lumen. This project is investigating the effects of such agents on adenosine 3'5-monophosphate (cAMP) and guanosine 3'5-monophosphate (cGMP) metabolism in colonic epithelium and is exploring differences in the metabolism between the rapidly proliferating deep layers versus superficial colonic mucosa. Studies to date have demonstrated that the colon carcinogens N-methyl-N-nitro- N-nitrosoguanidine (MNNG) and N-methylnitrosourea (MNU) produce rapid increases in cGMP in full-thickness scrapings of colonic mucosa from humans, rats, and rabbits without concurrent acute increases in cAMP. MNNG and MNU also stimulate guanylate cyclase activity when added to homogenates of colonic mucosa, indicating that cGMP responses in intact cells reflect increased synthesis. Fatty acids and/or their oxidation products, which are found in increased concentrations in the colon of individuals on high-fat diets and may thus be cocarcinogenic factors of such diets, also activate guanylate cyclase of colonic mucosa. Since activation of this enzyme in colon and other tissues is mediated by oxidative or free radical mechanisms, it may be a target for the action of numerous carcinogens in their reactive forms. This effect in turn may be a factor in the initiation of the transformation process. Studies are in progress to examine the extent to which other carcinogens or cocarcinogens influence cyclic nucleotide metabolism in colonic mucosa, the precise mechanisms by which the effects of MNNG and fatty acids on guanylate cyclase are expressed, and the characteristics of basal and carcinogen responsive cyclic nucleotide metabolism in superficial versus deep colonic epithelium.

Identifying number: R26 CA 17511
Principal investigator: Sherwood L. Gorbach
Institution: Tufts-New England Medical Center
Title: Diet and Its Effect on Enzymes Linked to Colon Cancer

Total FY79 obligation: $98,668
Nutrition allotment: 100%
Nutrition funding: $98,668

Total FY80 obligation: $101,311
Nutrition allotment: 100%
Nutrition funding: $101,311

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Rats initially fed a grain diet, then shifted to a beef diet, have shown significant increases in the activity of certain enzymes in the fecal bacterial flora, beta-glucuronidase, arylnitroreductase, and azoreductase. This increase in specific activity in these "sentinel enzymes" occurred within 20 days of starting the meat diet. Advanced age also had an effect on these fecal enzymes. The meat-fed animals maintained their high levels throughout 20 months of life, with further increases in the levels of beta-glucuronidase. In grain-fed animals, the levels of fecal enzymes remained low during the first few months of life, but then rose to high levels after 12 months, and remained high.

The carcinogen dimethylhydrazine caused an increase in betaglucuronidase activity in both groups of animals. However, no effect was observed on the levels of azoreductase or nitroreductase activity.

Oral feeding of Lactobacillus acidophilus had no effect on enzyme levels in grain-fed animals. In meat-fed animals, Lactobacilli lowered the activity of beta-glucuronidase and nitroreductase in the fecal flora. Results of these studies indicate that diet, age, carcinogens, and Lactobacilli supplements can influence the metabolic activity of the bacterial flora.

Identifying number: R26 CA 18651
Principal investigator: Bertram I. Cohen
Institution: Public Health Research Institute
Title: Effect of Sterols and Bile Acids on Colon Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Effect of Sterols and Bile Acids on Colon Cancer (continued)

Project description:

In order to define more precisely the importance of bacterial transformants, a study will be made of the effect of induced changes in their colonic concentrations in cancer development in rats given carcinogens. In addition, it is planned to investigate an important detoxifying mechanism in humans (sulfation) in retarding tumor development. Methods of altering the colonic concentration of the bacterial metabolites will be sought. The epithelial cell kinetics of subjects and rats with different colonic concentrations of bacterial metabolites will be investigated. From these studies methods for identifying patients with a high risk of developing cancer and development of means of decreasing this risk may be forthcoming.

Identifying number: R26 CA 18660
Principal investigator: Alan S. Morrison
Institution: Harvard University
Title: International Case-Control Study of Bladder Cancer

Total FY79 obligation: $103,982
Nutrition allotment: 50%
Nutrition funding: $51,991

Total FY80 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The investigators are evaluating the risk ratio and attributable risk of developing lower urinary tract transitional cell carcinoma associated with coffee drinking in geographical areas that vary with respect to exposure rates and ethnic composition. Simultaneously estimates will be made of the risk ratio of beverages with smoking, with ingestion of analgesics, with the ingestion of artificial sweeteners and bracken fern, and the risk associated with participating in certain occupations.

Identifying number: R26 CA 19171
Principal investigator: Thomas M. Mack
Institution: University of Southern California
Title: Case-Control Study of Carcinoma of the Pancreas

Total FY79 obligation: $110,028
Nutrition allotment: 50%
Nutrition funding: $55,014

Total FY80 obligation: $78,874
Nutrition allotment: 50%
Nutrition funding: $39,437

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The investigators are studying the epidemiology of cancer of the pancreas to formulate causal hypotheses and to identify groups at high risk of developing this tumor. The study is a case-control project to be performed in Los Angeles County. The questionnaire being used provides data on occupational history, smoking, diet, alcohol consumption, and medical history and treatment.

Identifying number: R26 CA 21681
Principal investigator: Peter Goldman
Institution: Harvard University
Title: Detection of Ultimate Carcinogens in the Colon

Total FY79 obligation: $99,512
Nutrition allotment: 100%
Nutrition funding: $99,512

Total FY80 obligation: N/A Terminated

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Diet and the metabolic activity of intestinal microflora have been linked to the incidence of colon cancer. Gnotobiotic rats will be fed diets containing the mutagen azoxymethane 1,2-dimethylhydrazine, and cycasin. The reversion to histidine independence, which indicates the mutagenic response in the Amer mutants, will be observed in the lower bowel and the feces. This research will aid in the development of a site-specific host-mediated assay for the detection of ultimate carcinogens within the colon and for elucidating in a preliminary way the factors governing their formation and disappearance.

Identifying number: R26 CA 22369
Principal investigator: Maria A. Correia
Institution: University of California, San Francisco
Title: Colonic Cytochrome P-450: Chemical Carcinogenesis Role

Total FY79 obligation: $73,870
Nutrition allotment: 100%
Nutrition funding: $73,870

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Chemical carcinogens ingested in the diet either as common food constituents or food additives or contaminants are believed to play a major etiological role in the increasing incidence of carcinoma of the colon in the developed countries. Many of these potential carcinogens undergo biotransformation (inactivation) at the site of their entry in the body or in the liver. Most of these inactivation reactions are catalyzed by microsomal mixed-function oxidase systems of which cytochrome P-450 and cytochrome P-450 reductase are essential components. Whereas the nature, function, and regulation of these oxidizing enzyme systems in the liver and, more recently, in the small intestine have been elucidated, little is known about the metabolism, biotransformation, and potential inactivation of ingested carcinogens and the role of possible cocarcinogens in the colonic mucosa, except that mixed-function oxidase activity has been identified in this tissue.

This project is designed to investigate the nature and activity and regulation of mixed-function oxidases and of their component cytochrome P-450 in the colonic mucosa of rats under a variety of experimental and nutritional conditions. Particular attention will be paid to evolving changes in the function and activity during chemically induced carcinogenesis. As with previous findings in the small intestine, cytochrome P-450 and mixed-function oxidase activity were found to occur in highest concentration primarily in the most mature cell populations of the mucosal surface. The findings are expected to elucidate the role of biotransformation mechanisms in the colonic mucosa in the production or prevention of cancer of the colon.

Identifying number: R26 CA 23760
Principal investigator: Basil C. Morson
Institution: St. Mark's Hospital
Title: Randomized Trial of an Antioxidant in Polyposis Coli

Total FY79 obligation: $33,220
Nutrition allotment: 100%
Nutrition funding: $33,220

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

The disease known as polyposis coli (adenomatous polyposis or familial polyposis) provides an excellent model for the study of both adenomas and cancers of the large bowel when these are present as adenomas and isolated lesions of the large bowel. In both settings, adenomas may be reversible.

Antioxidants retard experimental carcinogenesis and, in previous studies, administration of an antioxidant (ascorbic acid) to a few patients with polyposis coli was associated with a reduction in the number and size of adenomas in some individuals. These results, which have been duplicated, must be explained by either a pharmacologic effect or a cyclic variation in adenomas independent of drugs.

In this randomized, double-blind study, ascorbic acid or a placebo will be given to approximately 40 polyposis patients at St. Mark's Hospital in London. This is the only hospital in the world with access to sufficient patients for a definitive phase III study to investigate the chemoprevention of large bowel cancer.

Identifying number: R26 CA 23789
Principal investigator: Robert A. Squire
Institution: Johns Hopkins University
Title: Inhibition of Bladder Carcinogenesis by Retinoic Acid

Total FY79 obligation: $136,235
Nutrition allotment: 100%
Nutrition funding: $136,235

Total FY80 obligation: $146,663
Nutrition allotment: 100%
Nutrition funding: $146,663

Cancer activity/thrust: Preclinical Treatment/Treatment Research

Inhibition of Bladder Carcinogenesis by Retinoic Acid (continued)

Project description:

The potential inhibition of rat bladder carcinogenesis by 13-*cis*-retinoic acid will be studied. The carcinogen will be *N*-butyl-(4-hydroxybutyl) nitrosamine administered by gastric intubation twice per week for 6 weeks for a total dose of 1,200 mg. The retinoid will be given continuously in the feed at 300 mg/kg of diet, prior to, simultaneously with, and after carcinogen exposure.

Possible inhibitory effects will be evaluated by sequential observation throughout the animal's life span and by evaluation of the levels of DNA, RNA, and protein synthesis in the urothelium. Specific attention will be given to cell proliferation, tumor incidence, progression or reversibility, histologic grading, invasion, and metastases. In order to assess the feasibility and safety of 13-*cis*-retinoic acid as an antineoplastic agent, subchronic toxicity will also be assessed in a 180-day feeding study at doses of 300, 600, and 800 mg/kg of diet. Complete clinical, pathological, biochemical values and tissue bioaccumulation will be assessed.

Identifying number: R26 CA 23857
Principal investigator: Tracy D. Wilkins
Institution: Virginia Polytechnic Institute and State University
Title: Relation of Fecal Mutagens to Colon Cancer

Total FY79 obligation: $44,980
Nutrition allotment: 100%
Nutrition funding: $44,980

Total FY80 obligation: $47,226
Nutrition allotment: 100%
Nutrition funding: $47,226

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This project is concurrent with developing methods to assay, isolate, and identify mutagens in the fecal contents from individuals at low and high risk for colon cancer. Correlations between the excretion of mutagens and colon cancer will be sought using the Ames assay. The role of the intestinal microflora in forming, activating, or inactivating mutagens represents an important area of research that may lead to the development of a screening technique for people at high risk for colon cancer as well as the possible elucidation of the mutagenic (presumptive carcinogenic) agent.

Identifying number: R26 CA 24119
Principal investigator: Johannes Clemmensen/Ole Moller Jensen
Institution: Danish Cancer Registry
Title: Case-Control Study of Urinary Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Total FY80 obligation: $39,135
Nutrition allotment: 50%
Nutrition funding: $19,568

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The objective of this grant is to carry out a case-control study of cancers of the lower urinary tract: bladder, renal pelvis, and ureter. The investigators are studying the relationship between various environmental factors and the risk of cancer, and they are pursuing the possibility that there are significant interactions between the various risk factors. The application proposes to investigate the significance of tobacco consumption, coffee drinking, exposure to occupational carcinogens, use of artificial sweeteners and the use of various analgesic compounds.

Identifying number: R26 CA 24217
Principal investigator: John H. Weisburger
Institution: American Health Foundation
Title: Carcinogens and Mutagens in Colon Cancer

Total FY79 obligation: $68,491
Nutrition allotment: 100%
Nutrition funding: $68,491

Total FY80 obligation: $75,158
Nutrition allotment: 100%
Nutrition funding: $75,158

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Colon cancer is related to high consumption of beef/fat. Broiling of beef or pyrolysis of proteins and aromatic amino acids have been shown to yield mutagens, so that it seems possible that cooking of meat, leading to some pyrolysis of the outer surface, yields carcinogens responsible for these diet-related cancers. The effect of time, temperature, and method of cooking, such as frying and broiling, upon the production of mutagens in meat will be determined. Meat surface scrapings, homogenized in dimethylsulfoxide, will be assayed for mutagenicity, with the use of both the method of Ames with and without microsomal activation, and the method of Williams for induction of unscheduled DNA synthesis in rat liver-cell culture. Mutagens found in meat scrapings will be purified. With the purfication scheme of Sugimura et al., it can be demonstrated that the same mutagens they obtained from the pyrolysis of tryptophan are present in cooked meat.

A purification scheme in some other mutagens has also been devised. The amount of mutagen in the feces and urine of persons consuming their normal diet, broiled beef, boiled beef, and a vegetarian diet will be determined to see if an increase in mutagen content occurs when broiled beef is eaten. In addition, with the use of purification techniques for the isolation of mutagen from cooked meat, comparison of elution profiles of mutagen from the purification and from urine and fecal samples obtained from participants in the diet study, presumptive data can be obtained to show whether or not mutagens from broiled beef are present in the urine and feces.

Identifying number: R26 CA 25025
Principal investigator: Steven R. Tannenbaum
Institution: Massachusetts Institute of Technology
Title: Diet and Intestinal Formation of Nitrite in Humans

Total FY79 obligation: $123,584
Nutrition allotment: 100%
Nutrition funding: $123,584

Total FY80 obligation: $67,387
Nutrition allotment: 100%
Nutrition funding: $67,387

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Studies of nitrate balance in humans and analyses of fecal and ileostomy samples indicate that nitrite and nitrate are formed de novo in the intestine, possibly by heterotrophic nitrification. These findings significantly alter previous conceptions of human exposure to nitrite and suggest that nitrite may have a role in the etiology of intestinal cancer via the formation of carcinogenic N-nitroso compounds. In the proposed research, experiments will be conducted on humans to determine the effect of diet on formation of nitrite and *N*-nitroso compounds. These experiments will be performed on normal, healthy individuals, and on patients with ileostomies. The microbial formation of nitrite from ammonia will be studied and a determination will be made regarding whether dietary variables including fat, protein, fiber, ascorbic acid, and alphatocopherol influence the formation of nitrite and its reactivity.

Identifying number: R26 CA 25136
Principal investigator: Jen-Fu Chiu
Institution: University of Vermont and State Agricultural College
Title: Molecular Mechanisms in Large Bowel Carcinogenesis

Total FY79 obligation: $84,327
Nutrition allotment: 10%
Nutrition funding: $8,433

Total FY80 obligation: $73,375
Nutrition allotment: 10%
Nutrition funding: $7,338

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The major objectives of this project are to study the nature of genetic mechanisms in controlling colorectal epithelial cell proliferation and differentiation and the alterations in these mechanisms which accompany chemically induced neoplastic transformation. A small part of this project relates to studies of nuclear receptor protein for retinoids.

Identifying number: R26 CA 25157
Principal investigator: Lester Breslow
Institution. University of California, Los Angeles
Title: Colorectal Cancer Among California Mormons

Total FY79 obligation: $49,031
Nutrition allotment: 50%
Nutrition funding: $24,516

Total FY80 obligation: $80,881
Nutrition allotment: 50%
Nutrition funding: $40,441

Cancer activity/thrust: Epidemiology/Cause and Prevention

Colorectal Cancer Among California Mormons (continued)

Project description:

Based on analysis of church records, religiously active Mormon males in California and Utah compared with other U.S. white males have a standardized mortality ratio of 60 percent for colon cancer, 40 percent for rectal cancer, and 55 percent for colorectal cancer. Active Mormons abstain from tobacco, alcohol, and caffeine by church proscription; however, the specific reasons for their low colorectal cancer rates are unknown.

The first objective is to pursue this descriptive mortality data with a prospective epidemiologic study of active California Mormon adults of both sexes. With the use of a questionnaire survey, demographic, life style, dietary, occupational, and medical history data relevant to colorectal cancer etiology will be obtained on about 20,000 active Mormons, who will subsequently be monitored for mortality for 4 years. Furthermore, church-based mortality rates covering the years 1960-67 and 1976-79 will be ascertained for all 350,000 California Mormons in order to supplement the existing data for the years 1968-75. The questionnaire data on dietary and other lifestyle characteristics will be related to the colorectal cancer mortality rates. In addition to intra-Mormon comparisons, active Mormons as a whole will be compared with other California, U.S., and international populations that already have been studied with respect to colorectal cancer.

The second objective is to do a correlation analysis of extensive dietary and lifestyle data from the 1971-73 U.S. Health and Nutrition Examination Survey (HANES) with U.S. and California colorectal cancer mortality rates by country of birth and state of residence. Several etiologic variables of interest, including beef, fat, fiber, and beer consumption, will be examined for consistency with international correlations and previous epidemiologic findings. Special emphasis will focus on Spanish Americans born in Mexico, who have colorectal cancer death rates as low as those of active Mormons. The above analyses should yield new understanding of the etiology and prevention of large bowel cancer in the United States.

Identifying number: R26 CA 25509
Principal investigator: Neal K. Clapp
Institution: University of Tennessee, Knoxville
Title: Effects of Dietary Bran on Colon Cancer in Mice

Total FY79 obligation: $47,940
Nutrition allotment: 100%
Nutrition funding: $47,940

Total FY80 obligation: $47,475
Nutrition allotment: 100%
Nutrition funding: $47,475

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Epidemiological inferences and observations in humans indicate possible significance of dietary bran in inhibiting colon cancer in humans. Despite this, no studies have been performed with the use of well-characterized dietary bran to determine its effects on colon cancer induced in animals. This suggests the need for studies to determine carefully the relative effectiveness of various forms of dietary bran in inhibiting colon cancer with the use of animal models.

The objective of this research is to determine the relative effectiveness of four forms of well-characterized dietary bran: 1) corn bran, 2) soybean bran, 3) wheat bran from hard spring wheat, and 4) wheat bran from soft winter wheat, in inhibiting colon carcinogenesis in BALB/c mice treated with 1,2-dimethylhydrazine (DMH). BALB/c mice will be fed pelleted diets containing 20 percent bran beginning at 8 weeks of age; DMH will be injected at a rate of 20 mg/kg body weight weekly for 10 weeks beginning at 11 weeks of age following our previously described treatment regime. Mice will be held for approximately 40 weeks after initial injections at which time they will be killed. The evaluation of the relative effectiveness of these dietary brans in inhibiting colon carcinogenesis will then be made in terms of tumor incidence, numbers of tumors per tumor-bearing mouse, and classification and multiplicity of tumors per mouse.

These experiments should provide information regarding the possible role of dietary bran and the type(s) of bran most effective in modifying DMH-tumorigenesis. They should also indicate which might be of benefit prophylactically or therapeutically in humans.

Identifying number: R26 CA 25639
Principal investigator: Maryce M. Jacobs
Institution: University of Nebraska Medical Center
Title: Effect of Selenium on Colon Carcinogenesis

Total FY79 obligation $95,624
Nutrition allotment: 100%
Nutrition funding: $95,624

Total FY80 obligation: $83,880
Nutrition allotment: 100%
Nutrition funding: $83,880

Effect of Selenium on Colon Carcinogenesis (continued)

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The primary objective is to study the inhibitory effects of selenium (Na_2SeO_3) on the colon carcinogen, 1,2-dimethylhydrazine. Initially the acute toxicology of selenium as sodium selenite will be determined. With the use of these data, the doses of selenium will be selected for the chronic toxicology and carcinogenicity studies. All animal studies will use male Sprague-Dawley rats. Selenium will be provided ad libitum in the drinking water before, during, and/or after carcinogen administration. The rats will receive weekly subcutaneous injections of 20 mg DMH per kilogram body weight for 10 and 20 weeks.

At this center, the incidence of colon tumor in DMH-treated rats for 20 weeks was reduced from 87 percent to 40 percent by 4 ppm selenium in the drinking water. Additionally, the total number of colon tumors induced by DMH was reduced more than threefold by supplemental selenium.

This study will determine whether 1) preexposure to selenium delays the onset of tumors; 2) early stages of colon cancer induction can be inhibited by selenium; 3) colon cancer induction can be reversed by selenium; and 4) sister chromatid exchanges (SCE's) can be used to distinguish lymphocyte cultures from normal rats and from rats treated with DMH or DMH plus selenium. The answers to these questions will be explored with the use of the combined methods of gross and histopathological examination and by enzymatic and cytogenetic assays. Colonic tissue assays will include glutathione peroxidase, selenium, mucin changes, ATPase, beta-glucuronidase, and mixed-function oxidase activities. In blood, selenium, glutathione peroxidase, SGPT, alkaline phosphatase, and SCE levels will be measured. These multidisciplined analyses may provide potential markers for diagnosis of neoplastic condition of the large bowel.

Identifying number: R26 CA 25859
Principal investigator: Howard F. Mower
Institution: University of Hawaii, Manoa
Title: Microbiological Factors Contributing to Colon Cancer

Total FY79 obligation: $69,626
Nutrition allotment: 100%
Nutrition funding: $69,626

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Cancer activity/thrust: Carcinogensis/Cause and Prevention

Project description:

Chemical causes of colorectal cancer are being sought by the use of a bacterial mutagen assay to detect potential carcinogenic substances in human fecal samples. Mechanisms whereby diet and environmental effects, in particular beef consumption, alter the fecal mutagens, fecal transnitrosase and fecal nitrosohydrolase also will be sought.

Identifying number: R26 CA 25878
Principal investigator: Richard C. Rose
Institution: Pennsylvania State University/Hershey Medical Center
Title: Absorption of Chemical Carcinogens in the Colon

Total FY79 obligation: $51,183
Nutrition allotment: 25%
Nutrition funding: $12,796

Total FY80 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Cancer activity/thrust: Carcinogensis/Cause and Prevention

Project description:

The aim of this study is to gather information about the absorption of known chemical carcinogens by epithelia of the mammalian colon. Extensive literature exists concerning the intracellular actions of chemical carcinogens in producing cancer of gastrointestinal epithelia and other tissues. Little is known, however, about the absorption of carcinogens from the intestinal lumen into the lining epithelia, or the absorption of carcinogens from the lumen into the blood. The primary carcinogens of interest will be 2-acetylaminofluorene; dimethylamino-biphenyl; *N*-methyl-*N*-nitro-*N*-nitrosoguanidine; and 1,2-dimethylhydrazine.

This study will determine with reliable in vivo and in vitro techniques the mechanism of transport in the colon of four known carcinogens. Studies will be performed in vivo and in vitro to determine if net absorption or secretion takes place. Appropriate studies will indicate whether each carcinogen crosses the colonic mucosa by simple diffusion, facilitated transport, or some form of active transport. It will also determine the effects of bile acids and fatty acids on the transport of carcinogens across colon and into colon mucosal cells. Guinea pigs and rats will be the primary subjects of investigation. Some in vitro studies will be performed on human tissue removed at the time of surgery for purposes of comparison.

Absorption of Chemical Carcinogens in the Colon (continued)

Short of eliminating carcinogens from the environment, the most effective measure for reducing the incidence of cancer will be to limit entry of these substances into the body tissues. The information gathered may serve as a base from which to design experiments on specifically limiting gastrointestinal absorption of chemical carcinogens. Thus, results of this work might provide the basis for a new approach to controlling environmental carcinogenesis associated with dietary factors.

Identifying number: R26 CA 25886
Principal investigator: Frank E. Jones
Institution: Medical College of Wisconsin
Title: Chemoprevention of DMH-Induced Colorectal Neoplasms

Total FY79 obligation: $27,107
Nutrition allotment: 100%
Nutrition funding: $27,107

Total FY80 obligation: $32,349
Nutrition allotment: 100%
Nutrition funding: $32,349

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

It is necessary to identify agents that are capable of inhibiting carcinogenesis in the large bowel. Investigation into the mechanisms of colorectal carcinogenesis suggests that antioxidants may have such a capability: butylated hydroxyanisole (BHA) retards experimental large bowel carcinogenesis, and ascorbic acid (AA) ingestion is associated with a reduction in number and size of adenomas in patients with multiple polyposis. Human consumption of both of these agents has proven to be well tolerated. Toxicity studies have not demonstrated significant problems.

This study is designed to demonstrate the efficacy of AA and BHA given concurrently in chemoprevention of experimental large bowel cancer. The optimum dose of each agent is to be determined. Any advantage of oral (systemic) or rectal (local) administration will be determined, and the superior agent will be identified. Effects of AA and BHA in combination will be studied. In addition, toxicity will be documented.

First, AA and/or BHA will be administered orally or rectally in varying dosage to CF1 mice that are being given the large bowel carcinogen, 1,2-dimethylhydrazine. After 40 weeks, survival, tumor incidence and histology, and toxicity will be determined. Next, the procedure will be repeated in mice being fed only the minimum amount of food consumed by any group in experiment 1 in order to relate any growth effect of toxicity to dietary intake versus toxicity of the drugs. Third, the most effective dose of each agent and combination, as determined in experiment 1, will be administered to mice receiving DMH. Mice will be killed at intervals to determine the effect of AA and/or BHA on the rate of development of large bowel neoplasm.

Identifying number: R26 CA 25903
Principal investigator: Abraham M. Nomura
Institution: University of Hawaii, Manoa
Title: Mutagens and Lower Urinary Tract Cancer in Hawaii

Total FY79 obligation: $63,468
Nutrition allotment: 50%
Nutrition funding: $31,734

Total FY80 obligation: $66,158
Nutrition allotment: 50%
Nutrition funding: $33,076

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This case-control study will investigate the association of lower urinary tract cancer with chemical mutagens in the urine in two ethnically distinct groups in Hawaii which have different levels of risk for this disease (high risk for Caucasians and intermediate risk for Japanese). It will also include data on the association of this cancer with smoking cigarettes, drinking coffee, occupational exposures, and the use of artificial sweeteners.

Patients with cancer of the lower urinary tract will be identified in the seven major civilian hospitals in Oahu for 5 years (approximately 104 Caucasians and 92 Japanese). Surviving patients that were diagnosed within 2 years of the start of the study (30 Caucasians and 28 Japanese) will be recruited. For each, two neighborhood controls matched by race, sex, and age within 5 years will be selected and interviewed. Overnight urine samples for a battery of mutagen tests (Ames) will be collected from all subjects.

Mutagens and Lower Urinary Tract Cancer in Hawaii (continued)

The questionnaire and format for this study will be similar in design to an ongoing case-control study being conducted by the Harvard School of Public Health in three different populations (including the low-risk Japanese in Nagoya, Japan). This arrangement will permit a comparative analysis of findings of the Japanese in Hawaii and Nagoya to identify factors that account for the increase in lower urinary tract cancer among the Japanese in Hawaii. In addition, a comparative analysis will be made on data of the Caucasians and Japanese in Hawaii to identify factors that may account for the difference in risk between these two groups which reside on the same island.

Identifying number: R26 CA 25904
Principal investigator: Jimmie B. Vaught
Institution: Michigan Cancer Foundation
Title: Mechanisms of Phenacetin Carcinogenesis

Total FY79 obligation: $94,701
Nutrition allotment: 15%
Nutrition funding: $14,205

Total FY80 obligation: $101,887
Nutrition allotment: 15%
Nutrition funding: $15,283

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

These studies are designated to clarify the role of metabolic activation in the toxicity and carcinogenicity of phenacetin. Attempts will be made to alter the carcinogenic potential of phenacetin through metabolic manipulation and promotion by saccharin. These experiments should provide insight into the potential synergistic effects of these commonly encountered agents.

Identifying number: R26 CA 26362
Principal investigator: Dee W. West
Institution: University of Utah
Title: Bladder Cancer Risk Factors in Utah

Total FY79 obligation: $66,671
Nutrition allotment: 30%
Nutrition funding: $20,000

Total FY80 obligation: $83,914
Nutrition allotment: 30%
Nutrition funding: $25,174

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

Previous epidemiological studies have identified several risk factors in the etiology of bladder cancer, and a national study has been completed to determine whether these factors are associated with the disease. This was a case-control study in defined geographic areas with randomly selected population controls.

Residents of Utah participated in this 12-month study, but the number of cases identified in Utah in 12 months (127) will not allow adequate sample size to perform the multivariate analysis techniques needed to test several important hypotheses. Since coffee and tobacco consumption are low in the Utah population, hypotheses concerning these risk factors can be studied without the problems found in other populations where the groups of nonusers are small. In particular, coffee can easily be studied in Utah, as well as caffeine and the interaction of both with tobacco in the etiology of bladder cancer.

Urban-rural differences and an increasing incidence for older males have also been noted in the state and identification of risk factors for these findings may suggest new hypotheses. The plan will utilize the same design as in the national study, but more data will be collected on coffee consumption. This will be done for 2 years and an additional year will be necessary for data analysis.

Identifying number: R26 CA 26673
Principal investigator: Neal H. Stiegbigel
Institution: Montefiore Hospital and Medical Center, New York
Title: Association of Streptococcus Bovis With Colon Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $33,127
Nutrition allotment: 5%
Nutrition funding: $1,656

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The documented association of *Streptococcus bovis* fecal carriage and carcinoma of the colon and of *S. bovis* sepsis and occult colonic neoplasms prompt intensive investigation into these associations. The epidemiology of S. bovis will be further studied by obtaining fecal cultures from normal controls over time, from subjects on both standard and vegetarian diets, from patients with noncolonic gastrointestinal neoplasms, from patients with inflammatory bowel disease and from those with benign colonic polyps. Patients with S. bovis septicemia will undergo extensive gastrointestinal evaluations. Search will be undertaken for any particular biotypes of S. bovis carried by patients with colon cancer and for any serologic response by normals or colon cancer patients to the S. bovis carrier state. Studies of the adherence properties of S. bovis for normal colonic tissue and colonic neoplastic tissue will be undertaken. Sterile fecal filtrates from subjects will be examined for growth promoting factors for S. bovis.

Identifying number: R26 CA 26674
Principal investigator: Eleanor E. Deschner
Institution: Sloan-Kettering Institute for Cancer Research
Title: Modification of DMH-Induced Acute Response in Colon

Total FY79 obligation: N/A

Total FY80 obligation: $69,617
Nutrition allotment: 30%
Nutrition funding: $20,885

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

The acute response of colonic epithelial cells to 1,2-dimethylhydrazine delivered subcutaneously at a weekly dose level of 20 mg/kg body weight to CF_1 mice has been shown to induce a permanent alteration in the distribution of the major zone of DNA synthesis within some crypts 1 week following the fifth treatment. This coincides with the time when areas of focal atypism of microscopic adenomas are found. This proposal using histologic, autoradiographic, and enzymatic endpoints seeks to determine firstly if this response by colonic epithelial cells is elicited only by an organotropic carcinogen or if weekly injections of alkylating agents and antimetabolites such as cytoxan, bleomycin, 5-fluorouracil, hydroxyurea, and cytosine arabinoside induce similar alterations in cell proliferation. Secondly, mouse strains resistant to DMH (AKR/J, GR, and DMA/2) will be examined and the acute effect of DMH on their colonic epithelial cells compared with that found in the sensitive CF_1 strain. The effect of the ultimate carcinogen of DMH activation MAM on both DMH-sensitive (SWR/J and P/J) and resistant strains will also be studied, as well as the effect of pyrazole administered prior to MAM. Lastly, substaces such as selenium, zinc, β-sitosterol, lithocholic acid, deoxycholic acid, and vitamin C will be delivered prior to and during DMH and MAM treatment to determine if any modification of the acute reaction takes place and at which stage of the damage and repair cycle these dietary additives may operate.

Identifying number: R26 CA 27019
Principal investigator: Howard A. Reber
Institution: University of Missouri, Columbia
Title: The Pancreatic Duct Mucosal Barrier

Total FY79 obligation: N/A

Total FY80 obligation: $45,847
Nutrition allotment: 50%
Nutrition funding: $22,924

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Chronic ethanol consumption is associated with chronic pancreatitis and may predispose to pancreatic cancer. Bile reflux into the pancreatic ducts has also been implicated in the development of these diseases. The principal investigator has shown that the pancreatic ducts possess a barrier to the back diffusion of HCO_3, which is damaged by bile salts, ethanol, and other agents (e.g., aspirin). This increases the permeability of the ducts and may increase the vulnerability of the pancreas to various carcinogens.

The objectives of this research program are: 1) to determine the effects of bile salts, ethanol, and aspirin on pancreatic structure and function; 2) to investigate the mechanism by which aspirin is secreted in pancreatic juice; and 3) to explore the relevance of these observations to pancreatic cancer.

To accomplish these objectives, the following experimental models will be employed: (1) dogs with gastric and pancreatic fistulas, in which the chronic effects of ethanol and/or aspirin on pancreatic secretion will be studied; 2) an in vitro method of pancreatic duct perfusion in which the factors that govern the transport of bile salts, ethanol, and aspirin across the duct mucosa as well as the effects on mucosal function, will be studied; 3) cats in which pancreatic function will be studied using micropuncture techniques (these animals will have been maintained on ethanol and/or aspirin for several months prior to study); and 4) hamsters in which the effects of chronic administration of aspirin and/or ethanol on the development of pancreatic cancer will be studied.

Identifying number: R26 CA 27438
Principal investigator: Bertram I. Cohen
Institution: New York University
Title: Effects of Sterols and Bile Acids on Colon Cancer

Total FY79 obligation: $108,311
Nutrition allotment: 100%
Nutrition funding: $108,311

Total FY80 obligation: $102,083
Nutrition allotment: 100%
Nutrition funding: $102,083

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Colon cancer is a major medical problem in the United States today. It is the second leading cause of mortality with 52,000 deaths per year reported. The distribution of colon cancer, particularly its infrequency in Japan, its increase among Japanese immigrants to Hawaii, and the high incidence of this disease in North Americans and northwest Europeans indicates that an environmental factor is of etiological significance in the development of this disease. Furthermore, evaluation of the dietary habits of populations with different risks suggests that dietary factors, particularly high intake of dietary fat and beef, have a strong association with large bowel cancer. Populations in high-risk areas consume diets with large portions of fat and beef whereas people in low-risk areas consume diets which are low in these components but rich in vegetable protein. The goal of this research is to determine the roles played by sterols, bile acids, and their metabolites as either carcinogens, cocarcinogens, or inhibitors in large bowel cancer.

In order to define more precisely the importance of plant sterols, neutral sterols, bile acids, and their metabolites, the effect of induced changes of the colonic concentrations of these compounds on cancer development in rats given carcinogens will be studied. In addition, the possible retarding effect of plant sterols in large bowel cancer and the role of sulfation on colon cancer will be examined. Metabolites of neutral sterols and bile acid, such as cholesterol epoxide and iso-bile acids, will be studied to determine their possible role in colon carcinogenesis.

From these studies, it may become possible to identify patients at high risk of developing cancer and devise means of decreasing the risk.

Identifying number: R26 CA 28943
Principal investigator: Laurence Kolonel
Institution: University of Hawaii, Manoa
Title: Case-Control Study of Diet and Prostate Cancer in Hawaii

Total FY79 obligation: N/A

Total FY80 obligation: $88,965
Nutrition allotment: 100%
Nutrition funding: $88,965

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This study will examine the role of diet in the etiology of prostate cancer. The dietary heterogeneity of Hawaii's multiethnic population offers a special opportunity to conduct such a study. Three separate dietary components will be included in a case-control design: 1) fats, 2) cadmium/zinc, and 3) vitamin A.

Cases with a histologically confirmed diagnosis of prostatic carcinoma will be identified for the period 1978-1983 through major hospitals on the island of Oahu. Each case will be matched on age and sex with two population controls. A dietary history, specifically designed to assess the food components of interest to this study, will be administered by trained interviewers to each study subject at his home; in addition, a hair sample will be collected from each subject. A total of 486 cases and 972 controls will be interviewed over the 3-year period of the study.

Dietary intakes of fat (total fat, saturated fatty acids, etc.), trace elements (zinc and cadmium), and vitamin A (both the preformed vitamin and its precursors) will be computed from the food histories and compared between cases and controls. The cadmium and zinc content of the hair samples will be correlated with the results from the diet histories.

Few data are presently available on the possible association of diet and prostate cancer. This study should contribute useful information on that subject.

Identifying number: P01 CA 05826
Principal investigator: Joseph H. Burchenal
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Clinical Cancer Research Center

Total FY79 obligation: $1,675,198
Nutrition allotment: 4%
Nutrition funding: $67,008

Total FY80 obligation: $1,405,748
Nutrition allotment: 4%
Nutrition funding: $56,230

Cancer activity/thrust: Clincal Treatment/Treatment Research

Project description:

The objective of this project is to compare regular oral diets to total parenteral nutrition in children receiving chemotherapy and pelvic irradiation. Additionally, the effect of TPN on immunocompetence will be studied.

Identifying number: P01 CA 06373
Principal investigator: Brian MacMahon
Institution: Harvard University
Title: Cancer Epidemiology and Prevention Research Center

Total FY79 obligation: $582,697
Nutrition allotment: 5%
Nutrition funding: $29,135

Total FY80 obligation: $428,173
Nutrition allotment: 5%
Nutrition funding: $21,409

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

This program project grant is a study of the epidemiology of major human cancer, with the ultimate goal of developing knowledge that will lead to prevention of these diseases. Studies which relate to dietary factors involve coffee and artificial sweeteners in bladder cancer and alcohol use in pancreatic cancer.

Identifying number: P01 CA 11531
Principal investigator: Irwin D. Bross
Institution: Roswell Park Memorial Institute
Title: Core Program in Biometrics of Cancer Epidemiology

Total FY79 obligation: $54,348
Nutrition allotment: 5%
Nutrition funding: $2,718

Total FY80 obligation: N/A

Cancer activity/thrust: Epidemiology/Cause and Prevention

Project description:

The purpose of this study is to continue the strong core program in biometrical phases of cancer epidemiology.

Identifying number: P01 CA 11535
Principal investigator: Saxon Graham
Institution: State University of New York, Buffalo
Title: Social Epidemiology and Control of Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $985,419
Nutrition allotment: 75%
Nutrition funding: $739,064

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

We request renewal of support for this program of research in the social epidemiology and control of cancer. In the area of social epidemiology we would complete analyses on data already collected in the following areas: cancer of the testis, in which upstate New York cases and random controls are compared; cancer of the cervix among Buffalo and Kenmore residents as compared to a random sample of that population; cancer of the buccal cavity from cases and nonneoplastic controls at Roswell Park Memorial Institute; cancer at various sites in asbestos-mining areas and other residential areas in Quebec; and leukemia in patients with and without previous history of infectious hepatitis and other diseases. In addition, we wish to continue data collection on: a study comparing melanoma and control patients at Roswell Park Memorial Institute; women with and without cancer of the cervix who are patients at Martin Luther King, Jr. hospital and USC-Los Angeles County Hospital in Los Angeles; women in upstate New York with cancer of the cervix and their spouses with genitourinary cancers; and cancer of the buccal cavity, esophagus, stomach and larynx in Niagara, Erie, and Monroe Counties in New York State comparing patients reported from these areas to the tumor registry with neighborhood controls on diet, smoking, and alcohol consumption.

Because many measures which can prevent or control cancer are related to the epidemiology of those diseases and involve changes in behavior, we are interested in the social and behavioral factors associated with cancer control. Thus we wish to complete analyses of a 5-year followup of a smoking clinic program. In addition, we wish to analyze the results of random sample survey of central Buffalo blacks to ascertain the extent of, and factors associated with, obtaining routine cervical cytology screening, continue gathering similar data on Chicanos and blacks in Los Angeles hospitals, and gather new cancer control data in Erie County, New York.

Identifying number: P01 CA 12376
Principal investigator: Ernst L. Wynder
Institution: American Health Foundation
Title: Environmental Carcinogenesis

Total FY79 obligation: $587,179
Nutrition allotment: 60%
Nutrition funding: $352,307

Total FY80 obligation: $571,442
Nutrition allotment: 60%
Nutrition funding: $342,865

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

Nutritional aspects of breast cancer in humans and monkeys and in rats will be studied from the point of view of fat-related hormonal changes, including investigations of basic mechanisms. Attempts will be made to develop an animal model of prostatic cancer by initiation with direct injections of methylnitrosourea.

Identifying number: P01 CA 13556
Principal investigator: Nicholas L. Petrakis
Institution: University of California, San Francisco
Title: Genetic Epidemiology and Natural History of Cancer

Total FY79 obligation: $696,179
Nutrition allotment: 5%
Nutrition funding: $34,809

Total FY80 obligation: $572,014
Nutrition allotment: 5%
Nutrition funding: $28,601

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

Epidemiological and experimental studies of breast cancer will investigate host, agent, and environmental factors in order to trace the etiology and pathogenesis of this disease. Host factors will be investigated from the perspectives of genetics, cytopathology, physiology, and biochemistry. Carcinogenic agents may be secreted into the breast fluids of women, and the role of these agents in the initiation and promotion of breast cancer will be analyzed. Certain nutritional components of the environment and their possible role in breast cancer etiology will be explored. Also, health practices of women will be investigated with regard to early breast cancer detection.

These studies should engender new hypotheses for the etiology of breast cancer and help to predict more accurately the risk of breast cancer for asymptomatic women. Elucidation of processes of initiation and pathogenesis of breast cancer could lead to the development of preventive programs against this disease.

Identifying number: P01 CA 14294
Principal investigator: Kurt J. Isselbacher
Institution: Massachusetts General Hospital
Title: Tumor-Associated Changes of Intestinal and Liver Cells

Total FY79 obligation: $281,531
Nutrition allotment: 60%
Nutrition funding: $168,919

Total FY80 obligation: $280,607
Nutrition allotment: 60%
Nutrition funding: $168,364

Cancer activity/thrust: Cancer Biology/Cancer Biology

Tumor-Associated Changes of Intestinal and Liver Cells (continued)

Project description:

This program project will study various aspects of the behavior and characteristics of normal and malignant cells with a special emphasis on cells of the intestinal tract and liver. Major areas of investigation will include the following:

(1) Differences in transport of nutrients, especially sugars and amino acids, between normal and malignant fibroblast and epithelial cells. A major emphasis will be on possible surface membrane changes in relation to transport using the technique of measuring translocation across membrane vesicles and reconstituted vesicles (i.e., liposomes).

(2) The biological and clinical significance of a tumor-associated isoenzyme of galactosyltransferase activity found in the sera and tumors of animals and patients with malignant neoplasms. This isoenzyme and a recently detected serum inhibitor of galactosyltransferase activity found in animals with large tumors will be studied for their effects on cell growth in tissue culture systems and animal tumor models.

(3) The synthesis of surface glycoproteins and the role of lipid intermediates in glycoprotein synthesis.

(4) A tumor-associated alpha H_2-globulin, a recently described oncofetal protein, and tumor-associated isoferritins, will be purified from liver and intestinal tract tumors and characterized with the aim of developing antisera to these tumor-associated proteins that may be of diagnostic significance.

Identifying number: P01 CA 15823
Principal investigator: G. Barry Pierce
Institution: University of Colorado Medical Center
Title: Program in Developmental Biology of Cancer

Total FY79 obligation: $147,969
Nutrition allotment: 10%
Nutrition funding: $14,797

Total FY80 obligation: $330,595
Nutrition allotment: 10%
Nutrition funding: $33,060

Cancer activity/thrust: Cancer Biology/Cancer Biology

Project description:

This project includes studies of the effect of vitamin A on squamous endometrial cell differentiation in tissue and organ cultures.

Identifying number: P01 CA 16835
Principal investigator: Robert A. Kyle
Institution: Mayo Foundation
Title: Studies of Monoclonal Gammopathies in Humans

Total FY79 obligation: $144,997
Nutrition allotment: 10%
Nutrition funding: $14,500

Total FY80 obligation: $152,474
Nutrition allotment: 10%
Nutrition funding: $15,247

Cancer activity/thrust: Immunology/Treatment Research

Project description:

This is a multifaceted program to increase our understanding of the relationship between conditions associated with monoclonal gammapathies, the mechanism of immunodeficiency in multiple myeloma, cell kinetics in patients with monoclonal gammapathies, and the treatment of multiple myeloma bone disease with fluoride, calcium, and vitamin D.

Identifying number: P01 CA 19267
Principal investigator: Herbert F. Oettgen
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Clinical Immunobiology

Total FY79 obligation: $1,040,298
Nutrition allotment: 5%
Nutrition funding: $52,015

Total FY80 obligation: $975,452
Nutrition allotment: 5%
Nutrition funding: $48,773

Cancer activity/thrust: Immunology/Treatment Research

Project description:

This project includes studies on the levels and metabolism of iron, zinc, copper, chromium, and manganese and their role in immunologic disease. The use of nutrition support therapy in immunodeficiency diseases will also be investigated.

Identifying number: P01 CA 22484
Principal investigator: James A. Miller
Institution: University of Wisconsin, Madison
Title: Biochemical Studies in Chemical Carcinogenesis

Total FY79 obligation: $872,340
Nutrition allotment: 3%
Nutrition funding: $26,170

Total FY80 obligation: $872,697
Nutrition allotment: 3%
Nutrition funding: $26,181

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This project encompasses a broad fundamental approach to the chemistry, biochemistry, and biology of tumor initiation and promotion by chemicals.

The program includes major studies on the activation of chemical carcinogens, the interactions of ultimate carcinogens with cellular macromolecules, biochemical events associated with the promotion of initiated cells to the development of gross tumors, factors that affect the differentiation of cells and the progression and regression of neoplastic or preneoplastic cells, and the biological and biochemical diversity of preneoplastic and neoplastic lesions. The program includes investigations at the subcellular level, in cell culture, and in the whole animal.

Identifying number: P01 CA 22795
Principal investigator: Jack Fishman
Institution: Rockefeller University
Title: Specialized Center for Cancer Endocrinology

Total FY79 obligation: $838,845
Nutrition allotment: 10%
Nutrition funding: $83,885

Total FY80 obligation: $889,325
Nutrition allotment: 10%
Nutrition funding: $88,933

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

Radiometric methodology will be used to examine the biosynthesis and the principal metabolic pathways of estrogen and androgens in patients with breast, endometrial, and prostate cancer and compare these with suitable controls.

The impact of endocrine therapy on these transformations will be measured to see whether it correlates with the response to the treatment. Dietary alterations in control patients will be made to observe their effect on the direction of estradiol metabolism, in the expectation that such may disclose a relationship between diet and risk for cancer.

The receptor population of human breast, endometrial, and prostate tumor tissues will be measured with particular emphasis on the heterogeneity of the estradiol receptors. The receptor spectrum will be correlated with the clinical history of the patient.

Studies will be continued on the basic mechanisms of estradiol biosynthesis and the role of its metabolism in target tissues in the expression of its various biological activities. The biosynthesis and function of the novel acids will remain an active area of investigation.

Identifying number: P01 CA 23052
Principal investigator: Nathan O. Kaplan
Institution: University of California, San Diego
Title: Program Project on Athymic Mice and Human Tumors

Total FY79 obligation: $452,217
Nutrition allotment: 2%
Nutrition funding: $9,044

Total FY80 obligation: $761,515
Nutrition allotment: 2%
Nutrition funding: $15,230

Cancer activity/thrust: Cancer Biology/Cancer Biology

Program Project on Athymic Mice and Human Tumors (continued)

Project description:

An Athymic Mouse Research Facility has been established at the University of California, San Diego. The mouse colony contains close to 5,000 animals. Approximately one-half of them are used in experiments with transplantable human tumors. Twenty-seven human tumor lines are being maintained in the mice and in tissue cultures. This number is constantly increasing. Hormonal requirements of human tumors for growth in serum-free culture are being studied. The absence of serum in culture permits discovery of hitherto unsuspected hormonal dependence of these tumors. Clinical chemotherapy results on humans are correlated with those in mice or cell cultures. In these studies new and modified therapeutic agents (e.g., interferon and polymeric drugs) potentially useful in humans are being used. The effects of nutrition and growth requirements on human tumors are also explored.

Identifying number: P01 CA 23099
Principal investigator: Joseph V. Simone
Institution: St. Jude Children's Research Hospital
Title: Studies of Childhood Solid Tumors

Total FY79 obligation: $532,109
Nutrition allotment: 2%
Nutrition funding: $10,642

Total FY80 obligation: $848,064
Nutrition allotment: 2%
Nutrition funding: $16,961

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

Cancer is the leading cause of death from disease in children over 1 year of age in this country. Significant improvement has resulted from treatment regimens designed for the most common forms of childhood malignancy, acute lymphoblastic leukemia. Although progress in some of these solid tumors of children has been notable, such as in Wilms' tumor and Hodgkin's disease, the effectiveness of treatment regimens for most childhood tumors has been disappointing. In large part, the difficulties of disease control result from the fact that for many childhood tumors the disease has already disseminated beyond the site of origin at the time of diagnosis. Therefore, for most children with solid tumors a coordinated approach involving surgery, radiotherapy, and chemotherapy is necessary.

The role of chemotherapy is extremely important. This project will develop improved methods for treatment of neuroblastoma, osteosarcoma, and large bowel cancer. Both clinical and laboratory research will be brought to bear on these diseases. In addition to these specific disease categories, three general areas of research will be established and involve all patients with these tumors. These studies will include phase I and II programs for testing drugs, altered drug pharmacokinetics, and epidemiology.

Identifying number: P01 CA 23175
Principal investigator: Robert P. Gale
Institution: University of California, Los Angeles
Title: Bone Marrow Transplantation

Total FY79 obligation: $533,652
Nutrition allotment: 5%
Nutrition funding: $26,683

Total FY80 obligation: $526,760
Nutrition allotment: 5%
Nutrition funding: $26,338

Cancer activity/thrust: Immunology/Treatment Research

Project description:

A study will be made of the biology of bone marrow transplantation in animals and humans. It is divided into four major program areas: 1) clinical trials; 2) immunobiology of transplantation; 3) interstitial pneumonia; and 4) infectious disease.

Clinical trials are being conducted to study the role of transplantation in aplastic anemia, leukemia, and immunodeficiency diseases. Studies in progress include graft-rejection, graft versus host disease, leukemia eradication, and prophylaxis of infection and interstitial pneumonia. Phase-I trials are investigating fetal liver transplantation. A phase-II trial of autotransplantation is being conducted in patients with solid tumors.

The program in immunobiology is directed towards the following: 1) antigens on and immunity to hematopoietic stem cells, 2) in vitro models of immunity to nonmajor histocompatibility complex (MHC) antigens, and 3) in vitro induction of transplantation tolerance.

Studies of interstitial pneumonia include an animal model of latent cytomegalovirus (CMV) infection, in vitro studies of immune response to CMV and other viruses, and a clinical trial of CMV prophylaxis.

The program in infection prevention involves rapid diagnosis of fungal disease and the role of protected environments and granulocyte transfusions in transplantation.

Identifying number: P01 CA 23766
Principal investigator: Robert A. Good
Institution: Sloan-Kettering Institute for Cancer Research
Title: Marrow Transplantation in Aplastic Anemia and Leukemia

Total FY79 obligation: $887,925
Nutrition allotment: 2%
Nutrition funding: $17,759

Total FY80 obligation: $792,876
Nutrition allotment: 2%
Nutrition funding: $15,858

Cancer activity/thrust: Immunology/Treatment Research

Project description:

This is a coordinated multidisciplinary program of clinical and basic research on the biology of marrow transplantation as manifested in patients undergoing such transplantation for aplastic anemia and leukemia.

The studies in progress are designed to assess the contribution of various genetic, immunologic, and hematopoietic functions to engraftment, graft versus host disease, or increased susceptibility to infection. Immunogenetic analyses are designed to distinguish those alloantigenic systems inside and outside the major histocompatibility complex that must be common to donor and host if engraftment is to be regularly achieved and severe graft versus host disease avoided. Studies of hematopoietic function are principally concerned with the biological processes which enhance or limit regeneration of normal hematologic function in the transplant recipient. Similarly, studies of the process of immune reconstitution in the marrow transplant recipient are designed to determine those functions or dysfunctions of the lymphoreticular system of the host (including lymphocytes, phagocytes, and the organs in which they develop) which may limit engraftment and functional reconstitution and, conversely, those of the marrow graft which influence the development and clinical expression of graft versus host disease or complicating infections.

The patients participating in these studies are individuals with aplastic anemia or leukemia who receive transplants of marrow after treatment with standardized experimental courses of radiotherapy and/or chemotherapy for cytoreduction or immunosuppression. The clinical and experimental results of these studies will then be used as a reference base for the development and selection of new therapeutic protocols for randomized trials.

Identifying number: P01 CA 25100
Principal investigator: Sidney S. Mirvish
Institution: University of Nebraska Medical Center
Title: N-Nitroso Compounds

Total FY79 obligation: $576,038
Nutrition allotment: 10%
Nutrition funding: $57,604

Total FY80 obligation: $568,363
Nutrition allotment: 10%
Nutrition funding: $56,836

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Project description:

This program is planned to broaden current knowledge about carcinogenesis by N-nitroso compounds in three main areas: 1) N-nitroso compounds may be involved in the etiology of a significant fraction of human cancer; 2) N-nitroso compounds are capable of inducing tumors in specific organs of experimental animals, which are difficult or impossible to induce by other carcinogens, and 3) N-nitroso compounds may act as carcinogens (at least in part) by alkylating cell macromolecules (i.e., DNA) in a fairly direct fashion, with or without prior enzymatic activation.

Identifying number: P01 CA 26731
Principal investigator: Steven R. Tannenbaum
Institution: Massachusetts Institute of Technology
Title: Endogenous Nitrate Carcinogenesis in Man

Total FY79 obligation: N/A

Total FY80 obligation: $540,363
Nutrition allotment: 100%
Nutrition funding: $540,363

Cancer activity/thrust: Carcinogenesis/Cause and Prevention

Endogenous Nitrate Carcinogenesis in Man (continued)

Project description:

It is proposed to investigate the role that nitrite and N-nitroso compounds may play in the etiology of human cancer. The focus of the program is to determine the endogenous synthesis and flux of precursors of nitrite and nitrosatable N-compounds in the gastrointestinal tract of man, and the influence of diet on formation, stability, and reactivity of nitrite. A major goal is to develop an analytical approach to evaluation of the specific risk for an individual from endogenous nitrosation reactions. A second major goal is to develop information which will lead to dietary prevention of endogenous nitrosation. These studies will be conducted in man and experimental animals, and will integrate the skills of a wide variety of scientific disciplines.

Identifying number: P01 CA 26755
Principal investigator: Colin T. Campbell
Institution: Cornell University
Title: Nutrition and Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $528,245
Nutrition allotment: 100%
Nutrition funding: $528,245

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The relationship of nutrition and cancer will be explored in separate studies which focus on biochemical mechanisms, on influences of specific dietary components, including protein, carbohydrates, vitamins, and dietary fiber, and on development of epidemiological information.

Identifying number: P01 CA 27502
Principal investigator: Frank L. Meyskens
Institution: University of Arizona
Title: Vitamin A Program Project

Total FY79 obligation: N/A

Total FY80 obligation: $612,882
Nutrition allotment: 100%
Nutrition funding: $612,882

Cancer activity/thrust: Clinical Treatment/Treatment Research

Project description:

The overall goal of this research is to define the interaction of vitamin A and its synthetic derivatives (retinoids) with preneoplastic and neoplastic states. Our approach is to use advanced technology in a multidisciplinary nutritional cancer research effort in studies of:

a) Retinol and retinoic acid binding proteins;
b) polyamine biosynthesis and ornithine decarboxylase metabolism cellular nutrition and transcription;
c) zinc metabolism;
d) DNA replication;
e) immunological effects;
f) hepatic injury;
g) pharmacokinetics;
h) tumor biology; and
i) clinical oncology.

These studies will help identify the potential nutritional support that vitamin A and its derivatives would have in relation to cancer.

Identifying number: P01 CA 28103
Principal investigator: C. E. Butterworth, Jr.
Institution: University of Alabama
Title: Core Clinical Nutrition Research Center

Total FY79 obligation: $185,201
Nutrition allotment: 100%
Nutrition funding: $185,201

Total FY80 obligation: $203,518
Nutrition allotment: 100%
Nutrition funding: $203,518

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

This project is to organize a comprehensive clinical nutrition research unit or "center." The present department of nutrition sciences, supported jointly by three schools (community and allied health, medicine, and dentistry) will coordinate the interdisciplinary program.

The objectives are improved patient care and disease prevention through 1) better utilization of existing knowledge about nutrition, and 2) research to develop better methods for nutritional assessment, data analysis and health care delivery.

An administrative unit will be established along with five other centralized units or teams: 1) a laboratory to provide shared facilities for basic research and clinical support services, 2) a clinical nutrition support team, 3) an animal facility to support basic nutrition research and teaching using animal models of human disease, 4) an information service to combat fraud, waste, and misinformation, and 5) an international unit to promote understanding and exchange of information with students and scientists in other parts of the world. Although each component has identifiable major responsibilities, extensive interaction and collaboration will be required. The organization is designed to provide maximal efficiency of research, service, and training through enhanced personal contact, greater intellectual stimulation, use of shared resources, and coordinated effort.

Identifying number: P01 CA 29502
Principal investigator: Richard S. Rivlin
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Cooperative Core Lab and Nutrition Research

Total FY79 obligation: N/A

Total FY80 obligation: $180,105
Nutrition allotment: 100%
Nutrition funding: $180,105

Cancer activity/thrust: Nutrition/Cause and Prevention

Project description:

The objective of this application for a clinical nutrition research unit is to form a unified coherent program in nutrition for the purposes of advancing multidisciplinary research, upgrading the teaching of nutrition for medical students, physicians and other health professionals, and improving the clinical care of patients at our medical centers and in the population in general. The proposed Unit will become the major focus for all of the nutrition efforts of the participating institutions, i.e., Memorial Sloan-Kettering Cancer Center, the New York Hospital-Cornell Medical Center, and the Rockefeller University. Seven components will be developed in this collaborative program including research with human subjects and populations, laboratory investigations, research training, shared research facilities and services, education programs for medical students, physicians and paramedical personnel, nutritional support services, and public information activities.

Identifying number: N01 CP 01012
Principal investigator: Seymour Jablon
Institution: National Academy of Sciences
Title: Studies of Cancer Among Atomic Bomb Survivors

Total FY79 obligation: N/A

Total FY80 obligation: $195,700
Nutrition allotment: 5%
Nutrition funding: $9,785

Project description:

Ionizing radiation has been shown to induce cancer in man. The contractor will study how exposure to environmental host factors alters radiation-induced response. The contractor will conduct a collaborative, epidemiologic case-control investigation for several cancers, particularly tumors of the breast and lung among atomic bomb survivors.

Identifying number: N01 CP 01016
Principal investigator: Michael J. Burridge
Institution: University of Florida
Title: Bovine Leukosis Survey of Florida

Total FY79 obligation: N/A

Total FY80 obligation: $27,500
Nutrition allotment: 100%
Nutrition funding: $27,500

Project description:

This survey will seek to cover the following information on bovine leukosis incidence:

1) name and address of the herd owner;
2) approximate number, age, and sex of persons (family and workers) routinely exposed to the herd over the past 5 years;
3) geographic location of the herd by postal zip code and by county FIPS-NCI code;
4) herd size (number of animals) and production type (beef or dairy);
5) individual data on approximately 11,000 cattle from randomly selected herds throughout the state to include: age, breed, and sex;

Bovine Leukosis Survey of Florida (continued)

6) months in the herd;
7) sire and production records (when available); and
8) BLV test result.

Identifying number: N01 CP 01039
Principal investigator: Allan G. Manus
Institution: Litton Bionetics
Title: Holding Facility for Laboratory Animals

Total FY79 obligation: N/A

Total FY80 obligation: $201,512
Nutrition allotment: 50%
Nutrition funding: $100,756

Project description:

Provide holding facilities for large number of rats and fewer numbers of mice. Provide standard lab chow diets and prepare the carcinogen-containing and carcinogen-free diets. Determine the subchronic toxicity of specific diets and compounds. Administer the carcinogens, or other agents in the diet, by injection, gavage, skin painting, or implantation. Weigh the animals weekly for the first 16 weeks of a project and biweekly thereafter. Administer two types of diets: standard lab chow containing carcinogens and other agents; and chemically defined amino acid diets with and without carcinogens. Unless otherwise specified, all animals will be fed a standard commercial chow diet. House the animals in plastic shoebox cages and, unless otherwise specified, provide food and water ad libitum.

Identifying number: N01 CP 01050
Principal investigator: Martin Lipkin
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Cell Proliferation and Susceptibility to Cancer of the Large Intestine

Total FY79 obligation: N/A

Total FY80 obligation: $98,000
Nutrition allotment: 25%
Nutrition funding: $24,500

Project description:

Evaluate approximately 390 to 420 patients per year, perform sigmoidoscopic and colonoscopic examinations and obtain colonic biopsies from these patients for studies. The study will include low- and high-risk groups selected on the basis of individual family histories and dietary patterns.

Identifying number: N01 CM 02066
Principal investigator: Charles G. Moertel
Institution: Mayo Foundation
Title: Phase II-III Studies

Total FY79 obligation: $105,000
Nutrition allotment: 100%
Nutrition funding: $105,000

Total FY80 obligation: N/A Terminated

Project description:

The contract supports phase II studies in multiple cancer. One study involved randomized trial of the effects of vitamin C versus placebo in advanced cancer patients. The results of the study have been published in the New England Journal of Medicine.

Identifying number: N01 CP 05600
Principal investigator: Marsha I. Dawson
Institution: SRI International
Title: New Retinoids for Chemoprevention of Epithelial Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $158,971
Nutrition allotment: 100%
Nutrition funding: $158,971

Project description:

The purpose of this project is to synthesize new retinoids for potential use as chemotherapeutic agents. The approach will involve the synthesis of small quantities of retinoid compounds, including those with ring, side-chain, and polar terminus modifications.

Identifying number: N01 CP 05601
Principal investigator: Hans Kaegi
Institution: SRI International
Title: Synthesize Radiolabeled Retinoids

Total FY79 obligation: N/A

Total FY80 obligation: $165,899
Nutrition allotment: 100%
Nutrition funding: $165,899

Project description:

Synthesize, isolate, purify, analyze, store, package, and distribute a variety of radioactive retinoids which will differ in chemical structure, type of radiochemical label, position of label, and specific activity. Produce for each compound as a rule 5-50 mCi at specific activities of 1-10 Ci/mmole for tritium-labeled compounds and 50-100 mCi/mmole for carbon 14-labeled compounds. Furnish all compounds to users in a form directly suitable for research purposes without further purification. Provide to the project officer and ultimate users assay and analytical data on compounds. Maintain an accurate inventory of compounds. Prepare data sheets for ultimate users in addition to information as stated above which will indicate requirements for handling and storage of the compounds.

Identifying number: N01 CP 05602
Principal investigator: Marian R. Hicks
Institution: University of London
Title: Chemoprevention of Epithelial Cancer by Retinoids

Total FY79 obligation: N/A

Total FY80 obligation: $182,726
Nutrition allotment: 100%
Nutrition funding: $182,726

Project description:

Retinoids have been shown to have an inhibitory effect on skin tumor development. This study will focus on urinary bladder carcinogensis, using varying doses of a nitrosamine as the carcinogenic agent and retinoids, provided by NCI, as the inhibitor. Retinoids will be added to the feed, and long-term serial sacrifice studies will be performed to gather histopathological and microscopic evidence of tumor progression. Saccharin will also be used in the mice in order to test the antipromoting capacity of retinoids.

Identifying number: N01 CP 05603
Principal investigator: Sushma Palmer
Institution: National Academy of Sciences
Title: Assess Dietary and Nutritional Factors and Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $309,730
Nutrition allotment: 100%
Nutrition funding: $309,730

Project description:

Research in the last few decades has led to a plethora of confusing assertions concerning the relationship of diet and cancer. Except in a few cases, the scientific validity of these concepts has neither been critically examined nor communicated to the public. Furthermore, there is no clear understanding of the priorities and directions for future research. Therefore, it is proposed that the National Academy of Sciences critically assess the existing data concerning the possible relationship of dietary components (nutrients and toxic contaminants) and nutritional factors to the incidence of human cancer. A committee of approximately 14 members will be formed to: conduct a comprehensive review of the state of knowledge in this area; identify and summarize pertinent information that can be communicated to the scientific community and to the public; and identify gaps in the data base and develop components which present current information on the relationship between nutritional factors and cancer.

Identifying number: N01 CP 05605
Principal investigator: Lee W. Wattenberg
Institution: University of Minnesota
Title: Dose Response Studies on Phenolic Antioxidants

Total FY79 obligation: N/A

Total FY80 obligation: $137,443
Nutrition allotment: 100%
Nutrition funding: $137,443

Project description:

The long-term inhibitory effects of butylated-hydroxyanisole on benzo(a)pyrene-induced pulmonary adenoma formation in female mice will be studied. Research will center on the impact of varying BHA doses given to mice on tumor development. Other variables will include the addition of methionine and cysteine to the diet and the effect of

Dose Response Studies on Phenolic Antioxidants (continued)

varying the fat content within the feed. The dependence of glutathione-S-transferase activity and glutathione content upon BHA concentration in the diet will also be investigated.

Identifying number: N01 CP 05610
Principal investigator: Leonard J. Schiff
Institution: IIT Research Institute
Title: Bioassay Retinoid Activity by Tracheal Organ Culture

Total FY79 obligation: N/A

Total FY80 obligation: $164,666
Nutrition allotment: 100%
Nutrition funding: $164,666

Project description:

Bioassay new retinoid compounds by the tracheal organ culture assay. Hamster tracheal organ cultures provide an experimental assay system for determining whether new retinoids can alter epithelial cell differentiation and for measuring their toxicity. Under conditions of vitamin A deficiency, the tracheobronchial epithelial forms keratinized squamous metaplastic lesions but in the presence of active retinoids, the process of keratinization is reversed toward columnar ciliated and mucus secreting cells similar to those observed in vitamin A normal animals. Toxicity of retinoids will be evaluated in the same tracheal organ culture system by measuring both proteoglycan released into the culture medium and that remaining in the cartilage.

Identifying number: N01 CP 05616
Principal investigator: Benjamin Mason
Institution: Geomet Technologies
Title: Reports on Environmental Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $330,993
Nutrition allotment: 10%
Nutrition funding: $33,099

Project description:

Identify, gather, collate, and summarize existing data and information on the nature of exposure, its level and number of persons exposed to specified carcinomas, and suspect carcinogens they would be asked to investigate as well as to provide any information related to the regulatory status of these compounds they have been asked to examine. Provide responses on about 65 substances for the first 14 months and 50 new substances for the next 12 months. In the final 12 months, a complete review on about 50 new substances and partial reviews on approximately 75-100 substances contained in the prior periods will be undertaken by Geomet, Incorporated.

Identifying number: N01 CP 05621
Principal investigator: Carl G. Smith
Institution: University of Nebraska
Title: Causation in Intestinal Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $68,090
Nutrition allotment: 100%
Nutrition funding: $68,090

Project description:

Studies on developing methods and on causation factors in intestinal carcinogenesis. Induce a high incidence of colon cancer in mice and learn the possible modifying factors involved in the development of intestinal neoplasia.

Identifying number: N01 CP 05622
Principal investigator: J. Lawson
Institution: University of Nebraska
Title: Action of Tryptophan on the Bladder

Total FY79 obligation: N/A

Total FY80 obligation: $20,016
Nutrition allotment: 100%
Nutrition funding: $20,016

Action of Tryptophan on the Bladder (continued)

Project description:

Action of tryptophan on the bladder. Prepare N-hydroxy derivatives of tryptophan and certain metabolites and investigate their effect on bladder epithelial cell proliferation and neoplasia in the whole animal. The demonstration of positive results in either approach would go far to clarify the present confused state of the involvement of tryptophan and its metabolites in bladder carcinogenesis and would lead to a search for N-hydroxylated metabolites of DL-tryptophan in vivo and a consideration of their chemistry and biochemistry.

Identifying number: N01 CP 05627
Principal investigator: Barry Gold
Institution: University of Nebraska
Title: Activation and Transport of N-Nitrosamines

Total FY79 obligation: N/A

Total FY80 obligation: $53,723
Nutrition allotment: 50%
Nutrition funding: $26,861

Project description:

The currently accepted pathway for the metabolic activation of dialkyl- and alkyl-arylnitrosamines into reactive electrophilic species involves an initial a-hydroxylation. The resulting a-hydroxynitrosamines are unstable (none have been isolated) and are postulated to fragment spontaneously into alkanediazotic acids and aldehydes or ketones, depending on the structure of the parent nitrosamines. The objectives of this project are to obtain additional evidence to implicating the a-hydroxynitrosamines have sufficient stability to migrate from the cytoplasm where they are formed, penetrate the nuclear membrane, and alkylate the DNA within; determine the ability of nuclear enzymes to activate nitrosamines (via a-hydroxylation) into alkylating agents; and, finally, determine the contribution of target tissue enzymes, both soluble and membrane-bound, to the electrophilic activation of nitrosamines.

Identifying number: N01 CP 05628
Principal investigator: Diane F. Birt
Institution: University of Nebraska
Title: The Possible Influence of Diet in Carcinogenesis

Total FY79 obligation: N/A

Total FY80 obligation: $113,743
Nutrition allotment: 100%
Nutrition funding: $113,743

Project description:

The NCI carcinogenesis area is committed to scrutinizing possible environmental hazards and directs a major part of its programs to this goal. Included are the testing of various materials for carcinogenicity and fundamental studies in carcinogenesis. Selection of compounds for testing is jointly determined by NCI and the Eppley Institute, and testing capacity has been made available from time to time for compounds requiring urgent national attention. More fundamental studies are principally related to improved screening and testing methodologies but also include research in mechanisms of action and in the chemistry and pharmacology of metabolized carcinogens and related compounds.

Identifying number: N01 CP 05715
Principal investigator: William H. Okamura
Institution: University of California, Riverside
Title: Retinoids for Chemoprevention of Epithelial Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $86,312
Nutrition allotment: 100%
Nutrition funding: $86,312

Project description:

The initial phase of the study will focus on the synthesis of side chain allenic retinoids. In the second phase, rearrangement studies of the allens via sigmatrophic or catalyzed reactions will be pursued. Alkylated, ring-fused, and other analogs will be pursued. The 7, 8 - allens and their rearrangement reactions will be pursued in the third phase, and, finally, the 6, 7 and 10, 11--allens. The primary goal is to investigate systematically the possibility that allenic and acetylenic groups might impart useful cancer prophylactic properties to the retinoids.

Identifying number: N01 CP 05716
Principal investigator: John E. McMurry
Institution: Cornell University
Title: New Retinoids for Chemoprevention of Epithelial Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $104,593
Nutrition allotment: 100%
Nutrition funding: $104,593

Project description:

The purpose of this project is to synthesize new retinoids for potential use as chemotherapeutic agents. The approach will involve the synthesis of small quantities of cycloretinoid derivatives in which various of the polyolefin side chain double bonds are held in specific conformations. Attention will also be placed initially on the synthesis of bicyclic aromatic analogs of retinoic acid.

Identifying number: N01 CP 05717
Principal investigator: Clifford W. Welsch
Institution: Michigan State University
Title: Supply Chemoprevention Retinoids for Epithelial Cancer

Total FY79 obligation: N/A

Total FY80 obligation: $74,969
Nutrition allotment: 100%
Nutrition funding: $74,969

Project description:

This investigation has two main objectives. The first is to study how concurrent hormone suppression and/or immune stimulation enhances the mammary tumorigenic-suppressive activities of retinoids in the carcinogen-treated Sprague-Dawley rat. The second thrust is designed to evaluate the mammary tumorigenic-suppressive activities of retinoids in three distinctly different types of mouse mammary carcinoma models.

Identifying number: N01 CP 05718
Principal investigator: Richard C. Moon
Institution: IIT Research Institute
Title: Chemoprevention of Epithelial Cancer by Retinoids

Total FY79 obligation: N/A

Total FY80 obligation: $139,846
Nutrition allotment: 100%
Nutrition funding: $139,846

Project description:

Determine which retinoids are highly effective in inhibiting N-methyl-N-nitrosourea (MNU)-induced mammary carcinogenesis. Determine the time interval that may elapse either before or after the carcinogenic insult without impairing the efficacy of the retinoid as regards mammary carcinogenesis. Determine the efficacy of retinoids relative to hormone dependency of the tumors. The efficacy of the retinoid in inhibiting mammary carcinogenesis will be assessed by evaluating the following parameters of mammary carcinogenesis: percent incidence mammary cancer and benign mammary tumors; number of mammary cancers and benign tumors; number of invasive tumors; number of mitotic figures; and latent period of tumor appearance.

Identifying number: N01 CP 05721
Principal investigator: Bandaru S. Reddy
Institution: American Health Foundation
Title: Dose Response Studies on Phenolic Antioxidants

Total FY79 obligation: N/A

Total FY80 obligation: $116,272
Nutrition allotment: 100%
Nutrition funding: $116,272

Project description:

This project designed to investigate the efficacy of inhibition of butylated hydroxytoluene on 1) azoxymethane-induced intestinal carcinogenesis in male rats and 2) methylazoxymethanol acetate-induced colon carcinogenesis in female mice. Varying doses and regimens will be explored.

Identifying number: N01 CP 05722
Principal investigator: Leonard Cohen
Institution: American Health Foundation
Title: Dose Response Studies on Phenolic Antioxidants

Total FY79 obligation: N/A

Total FY80 obligation: $93,345
Nutrition allotment: 100%
Nutrition funding: $93,345

Project description:

Studies of inhibition of mammary gland carcinogenesis by phenolic antioxidants will be carried out. The efficacy of particular doses and regimens of butylated hydroxyanisole and butylated hydroxytoluene will be evaluated.

Identifying number: N01 CP 05723
Principal investigator: Gray M. Williams
Institution: American Health Foundation
Title: Dose Response Studies on Phenolic Antioxidants

Total FY79 obligation: N/A

Total FY80 obligation: $109,040
Nutrition allotment: 100%
Nutrition funding: $109,040

Project description:

This study is intended to investigate the inhibitory effect of butylated hydroxytoluene on _N_-2-fluorenyl-acetamide-induced hepatocarcinoma of the rat. Varying levels of BHT and FAA will be used in the study. In addition, a technique using rat livers will be tested regarding its effectiveness as a rapid method for the assessment of chemopreventive efficacy of modifiers and inhibitors.

Identifying number: N01 CM 07334
Principal investigator: Tex Montgomery
Institution: University of Iowa
Title: Analysis of Proteinaceous Substances

Total FY79 obligation: N/A

Total FY80 obligation: $104,747
Nutrition allotment: 20%
Nutrition funding: $20,949

Project description:

The DCT, NCI, is engaged in the discovery and development of new substances with potential as antitumor agents. The search for new substances includes both synthetic and naturally occurring compounds of diverse structure. Developmental activities include preparation of significant quantities, analysis of these substances, and development and production of injectable pharmaceutical dosage forms. Further development and evaluation of these substances in larger animals and ultimately in man requires characterization of these agents. Suitable qualitative and quantitative methods must be developed to ascertain the purity and quality of this material from batch to batch in both bulk form and pharmaceutical dosage forms. About two or three compounds will require characterization annually. Most compounds will be proteinaceous and may include largomycin, interferon, lentanin, etc.

Identifying number: N01 CM 07344
Principal investigator: Gideon J. Luande
Institution: Muhimbili Medical Center
Title: Chemoprevention of Skin Cancer in Albinos

Total FY79 obligation: N/A

Total FY80 obligation: $125,000
Nutrition allotment: 100%
Nutrition funding: $125,000

Project description:

This project entails two tasks: a descriptive study of the demography and clinical features of albinos; and a clinical trial using retinoids to prevent skin cancer among this susceptible population.

Identifying number: N01 CP 22064
Principal investigator: Lee J. Wilkoff
Institution: Southern Research Institute
Title: Organ Culture and Tissue Culture Bioassay of Vitamin A Analogs

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Organ Culture and Tissue Culture Bioassay of Vitamin A Analogs (continued)

Total FY80 obligation: N/A Terminated

Project description:

The purposes of this project are to develop bioassays for evaluating retinoids, as measured by control of epithelial differentiation; to develop new assays for retinoid activity in organ or tissue culture; to evaluate the various aspects of the toxicity and pharmacology of retinoids in rodents; and to investigate the biochemical changes caused by carcinogens and their possible reversal by retinoids. With the use of N-methyl-N'-nitro-N-nitrosoguanidine-induced hyperplasia of mouse prostate explants as a tool, it was found that the methylketo and 1-methoxyethyl analogs of retinoic acid were 50-fold more active than retinoic acid in reversing the effect of the carcinogen. Other analogs were less active although still more effective than retinoic acid. A retinoic binding protein is present in various epithelial tissues; larger amounts are present in the tissues of young animals compared with older ones. However, serum albumin is the protein actually involved in transport of retinoic acid and its analogs. Serum albumin binds 13-cis-retinoic acid quite firmly, which may account for the low toxicity of the cis acid, but this also prevents the diffusion of cis-retinoic acid into cells.

Identifying number: N01 CP 23213
Principal investigator: Mitsuo Seigi
Institution: AICHI Cancer Research Institute
Title: Shifts in Cancer Risks Among Japanese Migrants

Total FY79 obligation: Active, not funded
Nutrition allotment: 40%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

Over the past several years, this project in Japan has included case-control studies on cancers of the esophagus, stomach, large bowel, lung, prostate, and breast. All of these studies related to the GI tract have included dietary surveys. The esophageal cancer studies showed a close relationship between mortality rate and the consumption of rice-tea gruel. The stomach cancer studies showed a protective effect for lettuce and celery but did not reproduce the association of stomach cancer with consumption of salted/dried fish and salt-pickled vegetables described for Japanese in Hawaii. The colon cancer data are being analyzed at the present time. In Akita Prefecture, collaborative studies are continuing on stomach cancer and colon cancer with the use of the same dietary questionnaire as in the Japan-Hawaii Cancer Study at the Kuakini Medical Center in Honolulu.

Identifying number: N01 CP 23292
Principal investigator: Richard C. Moon
Institution: IIT Research Institute
Title: Study of Modulating Factors in Carcinogenesis

Total FY79 obligation: $499,210
Nutrition allotment: 100%
Nutrition funding: $499,210

Total FY80 obligation: $320,000
Nutrition allotment: 100%
Nutrition funding: $320,000

Project description:

The respiratory tumor model as described by Schreiber for producing lesions in a circumscribed area of the trachea will be developed. The catheter and supportive equipment will be fabricated and modified to make it adaptable for use with large numbers of animals and those of different ages. A study will be made of the effects of anticarcinogenic agents, such as vitamin A analogs, on the progression of initiated tumors to detectable and lethal tumors of epithelial tissues in addition to those of the respiratory tract.

Identifying number: N01 CP 33235
Principal investigator: J. Wister Meigs
Institution: Yale University
Title: Support for Cancer Epidemiology Program

Total FY79 obligation: $421,000
Nutrition allotment: 10%
Nutrition funding: $42,100

Total FY80 obligation: $593,110
Nutrition allotment: 10%
Nutrition funding: $59,311

Support for Cancer Epidemiology Program (continued)

Project description:

This study is an 18-month project designed to provide the Commissioner of Food and Drugs with an answer to the question: Does saccharin initiate or promote human bladder cancer? The study employs a population-based case-control design. All newly diagnosed carcinomas of the urinary areas will be studied. It is estimated that there will be approximately 3,200 cases. In addition, 6,400 controls will be drawn as a stratified random sample of the general population.

In addition to saccharin ingestion, other exposures will be assessed: occupation, cigarette smoking, source of drinking water, coffee consumption, and intake of liquids. Assessment of historical and current drinking water quality is being made in cooperation with the Environmental Protection Agency.

Identifying number: N01 CP 33238
Principal investigator: Adrianne E. Rogers
Institution: Massachusetts Institute of Technology
Title: Chemical Carcinogenesis: A Bioassay System

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project is studying the effects of carcinogens in diets which provide adequate levels of nutrients for growth of rats but which are marginally deficient in the lipotropes choline, methionine, and folic acid and are high in fat. These diets simulate those consumed by many people. Under these conditions five of six carcinogens tested induced liver or colon tumor more rapidly but decreased the induction of other types of tumors. In some cases the enhanced induction of tumors could be decreased by supplementing the diet with the lipotropes or certain amino acids; with other carcinogens this did not occur.

Identifying number: N01 CP 33278
Principal investigator: David B. Clayson/Parviz M. Pour
Institution: University of Nebraska Medical Center
Title: Bioassays of Environmental Carcinogenesis

Total FY79 obligation: $2,530,750
Nutrition allotment: 5%
Nutrition funding: $126,537

Total FY80 obligation: Active, not funded
Nutrition allotment: 5%
Nutrition funding: None

Project description:

As part of the NCI commitment to investigate possible environmental hazards, various materials are being tested for carcinogenicity, including saccharin and cyclamates. Compounds for testing are selected jointly by NCI and the Eppley Institute, and testing capacity has been made available for compounds requiring urgent national attention. More fundamental studies are designed primarily to improve screening and testing methodologies, but include research in mechanisms of action and in the chemistry and pharmacology of metabolized carcinogens and related compounds. Advanced training is also included in this project to increase the number of competent investigators.

Identifying number: N01 CP 33286
Principal investigator: Carlos Cuello
Institution: Fundacion Para La Educacion Superior, Cali, Colombia
Title: Geographical Pathology and Epidemiology of Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 25%
Nutrition funding: None

Total FY80 obligation: $50,692
Nutrition allotment: 25%
Nutrition funding: $12,673

Project description:

The objectives of this project are to determine site-specific cancer incidence in Cali and other cities in Colombia, to correlate the morbidity data with pathology findings, and to conduct epidemiological studies of specific sites based on leads suggested by these data. Cancer incidence data are produced annually for the city of Cali and part of Medellin. Research on large bowel cancer has progressed to a comparative pathology study of precancerous lesions in three cities with differing cancer risks. A major study of cervical cancer and precancerous lesions in the Cali population is now in the analytical phase.

Geographical Pathology and Epidemiology of Cancer (continued)

In the Department of Narino in the southern part of Colombia, the comprehensive epidemiologic study of stomach cancer has revealed strong clustering of cases that may be associated with nitrates in water supplies and selected food items. The observational situation is very favorable for pursuit of diet and stomach cancer relationships. Three major papers based on this research were published describing in detail the cancer risk associated with suspected environmental agents, and case-control studies of precursor lesions. The current studies are focused on precancerous lesions, such as chronic atrophic gastritis and intestinal metaplasia, and their relationships to nitrate and nitrite levels in the gastric juice. The data so far indicate that patients without mucosal atrophy have lower pH values and minimal nitrite levels in their gastric juice, while patients with atrophy and/or intestinal metaplasia have a high pH and high nitrite levels. It appears that pH levels above five associated with mucosal atrophy are the main determinants of high nitrite levels that could eventually be converted to N-nitroso compounds. The potentially beneficial effects of vitamins A, C, and E based on their antioxidant properties are being evaluated in a group of patients with gastrointestinal symptoms.

Identifying number: N01 CP 33315
Principal investigator: Steven R. Tannenbaum
Institution: Massachusetts Institute of Technology
Title: Environmental Occurrence of N-Nitroso Compounds

Total FY79 obligation: $50,605
Nutrition allotment: 100%
Nutrition funding: $50,605

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

Nitrate enters the food supply from food additives, nitrate-contaminated water supplies, and vegetables grown in heavily nitrated fields. The aim of this study is to determine whether or not a direct relation can be established between formation of nitrite from nitrates in the human stomach and gastric cancer. The types of studies to be conducted are as follows: characterization of the gastric contents of individuals from a high-risk area; identification of factors controlling rate of nitrosation in human gastric juice; and characterization of mutagenic N-nitroso compounds formed from Colombian foods.

Identifying number: N01 CP 33325
Principal investigator: Leonard M. Schuman
Institution: University of Minnesota
Title: Research on Cancer Among U.S.-Born Norwegian Descendents

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project is the migrant part of the Norwegian migrant studies. Case-control studies have been conducted of gastrointestinal cancers among persons of Norwegian descent in Minnesota, and a cohort of approximately 20,000 people is being monitored. In the two countries combined, close to 40,000 persons responded to the mailed dietary questionnaire. Early results from Minnesota and Norway indicated that total vegetable intake and an index for vitamin C are negatively associated with stomach cancer. This relationship appears to be strongest among younger patients and women. Frequent use of cooked cereals among stomach cancer patients has also been noted. These studies indicate that frequent use of salted fish may be associated with an increased risk of stomach cancer in Norway. It has been suggested that changes in food preservation such as refrigeration may influence the prevention of this disease.

With respect to colorectal cancers, the situation is less clear. There is agreement that high-vegetable diets may be beneficial, but data on meat intake may not agree with other noted studies. It appears that there may be no effect on colorectal cancer related to beef intake, but a positive association may be found with processed meats, such as sausage.

Identifying number: N01 CP 33364
Principal investigator: Lee W. Wattenberg
Institution: University of Minnesota, St. Paul
Title: Polycyclic Hydrocarbon Metabolism

Total FY79 obligation: $145,000
Nutrition allotment: 10%
Nutrition funding: $14,500

Total FY80 obligation: Active, not funded
Nutrition funding: 10%
Nutrition allotment: None

Polycyclic Hydrocarbon Metabolism (continued)

Project description:

This project is to determine the relationship between activity and composition of the aryl hydrocarbon hydroxylase system, the metabolism of polycyclic hydrocarbons, and the binding of metabolites of polycyclic hydrocarbons to the macromolecular pulmonary structure. Chemical structural requirements for compounds such as BHA, BHT, and vitamin C to act as inhibitors of carcinogen-induced pulmonary neoplasia will be investigated.

Identifying number: N01 CP 43247
Principal investigator: Einar Pedersen
Institution: Norwegian Public Health Service
Title: Shifts in Cancer Risks Among Norwegian Migrants

Total FY79 obligation: Active, not funded
Nutrition allotment: 75%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project in Norway is the basic part of the Norwegian migrant study conducted in collaboration with Dr. Schuman at the University of Minnesota. In the two countries combined, close to 40,000 persons responded to the mailed dietary questionnaire. Early results from Minnesota and Norway indicated that total vegetable intake and an index for vitamin C are negatively associated with stomach cancer. This relationship appears to be strongest among younger patients and women. Frequent use of cooked cereals among stomach cancer patients has also been noted. These studies indicate that frequent use of salted fish may be associated with an increased risk of stomach cancer in Norway. It has been suggested that changes in food preservation such as refrigeration may influence the prevention of this disease.

Identifying number: N01 CP 43337
Principal investigator: C.L. Walters
Institution: British Food Manufacturing Industries Research Association
Title: N-Nitroso Compounds and Precursors in the Environment

Total FY79 obligation: $55,558
Nutrition allotment: 10%
Nutrition funding: $5,556

Total FY80 obligation: $43,064
Nutrition allotment: 10%
Nutrition funding: $4,306

Project description:

This project relates to development of analytic methods for determination of N-nitroso compounds in various types of foodstuffs.

Identifying number: N01 CP 43350
Principal investigator: Charles P. Angel
Institution: Tracor Jitco
Title: Carcinogenesis Testing, Bioassays Prime Contract

Total FY79 obligation: $13,248,424
Nutrition allotment: 1%
Nutrition funding: $132,484

Total FY80 obligation: $2,142,953
Nutrition allotment: 1%
Nutrition funding: $21,430

Project description:

This project supports bioassay of potentially carcinogenic agents which may include food additives or contaminants.

Identifying number: N01 CP 43382
Principal investigator: Joseph L. Lyon
Institution: University of Utah
Title: Epidemiological Investigation of Cancer in Utah

Total FY79 obligation: $163,215
Nutrition allotment: 25%
Nutrition funding: $40,803

Total FY80 obligation: $463,033
Nutrition allotment: 25%
Nutrition funding: $115,758

Epidemiological Investigation of Cancer in Utah (continued)

Project description:

Information is collected from hospitals, physicians, pathology laboratories, radiotherapy centers and the Utah State Division of Health and is processed quarterly by computer. Data being collected include diagnosis, treatment, and dietary information on subjects in the study.

Identifying number: N01 CP 53500
Principal investigator: Murray B. Gardner
Institution: University of Southern California
Title: Etiology and Epidemiology of Human Cancer

Total FY79 obligation: $271,000
Nutrition allotment: 10%
Nutrition funding: $27,100

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Project description:

The epidemiologic data being collected include dietary information on subjects in the study.

Identifying number: N01 CP 53511
Principal investigator: Lawrence H. Piette
Institution: University of Hawaii, Manoa
Title: Demographic Cancer Research Program in Hawaii

Total FY79 obligation: $1,220,297
Nutrition allotment: 10%
Nutrition funding: $122,030

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Project description:

Demographic/epidemiologic programs will be done in collaboration with the basic science and clinical research programs of the Cancer Center of Hawaii. Case-control interview work on Japanese migrant studies is in this program. Data being collected include dietary information on subjects in the study.

Identifying number: N01 CP 53521
Principal investigator: Pelayo Correa
Institution: Louisiana State University Medical Center, New Orleans
Title: Epidemiology and Geographic Pathology of Cancer

Total FY79 obligation: $164,238
Nutrition allotment: 50%
Nutrition funding: $82,119

Total FY80 obligation: $150,000
Nutrition allotment: 50%
Nutrition funding: $75,000

Project description:

The objectives of this project are to study colorectal polyps and their correlation with atherosclerosis and steroid metabolism; to conduct in vitro and in vivo experiments on the inhibition of nitrogen-containing mutagens; to collaborate on related studies in Colombia; and to develop collaborative efforts in other Latin American countries. A good correlation has been found between the prevalence of adenomatous polyps and colon cancer risks in several communities. Information on the correlation between polyps and atherosclerosis should be available next year and may implicate certain dietary factors associated with both diseases. Dr. Correa may soon start a study of fecal mutagens in polyp-bearing and polyp-free individuals. Another study has indicated that these mutagens are directly affected by the type of food consumed. Dr. Correa is one of the key investigators on the stomach cancer study in Colombia which includes a search for dietary factors associated with premalignant lesions in the stomach. Experiments on the inhibition of nitrogen-containing mutagens are now focused on spermidine nitrosation within the stomach.

Identifying number: N01 CB 53883
Principal investigator: Baruch Modan
Institution: Chaim Sheba Medical Center Tel Hashomer, Israel
Title: Correlation of Diet Epidemiology of Breast Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

A case-control study will be made in Israel over 3 years to determine whether dietary components, particularly fats and (low) cellulose, may serve as risk factors in the etiology of breast cancer. A validated questionnaire will be used to elicit the dietary information, including differential anthropometric measurements. The population to be studied will be composed of 500 newly diagnosed breast cancer patients of whom 300 will be European and American born and 200 will be Asian-African born and include 1,000 controls. Controls will be matched to patients on age, parity, menarche, country of origin, and period of immigration to Israel. Pathology slides will be collected for possible future studies. Analysis will be performed separately for the two main ethnic groups as well as for pre- and postmenopausal women.

Identifying number: N01 CB 53884
Principal investigator: Abraham M. Nomura
Institution: University of Hawaii, Manoa
Title: Role of Diet and Noncontraceptive Estrogens in Breast Cancer

Total FY79 obligation: $97,011
Nutrition allotment: 50%
Nutrition funding: $48,506

Total FY80 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Project description:

This study is to determine in postmenopausal women if there is an association of breast cancer with specific dietary factors and the use of menopausal estrogens.

Identifying number: N01 CP 55685
Principal investigator: Tracy D. Wilkins
Institution: Virginia Polytechnic Institute and State University
Title: Relation of Fecal Neutral Sterols to Large Bowel Cancer

Total FY79 obligation: $162,828
Nutrition allotment: 20%
Nutrition funding: $32,565

Total FY80 obligation: Active, not funded
Nutrition allotment: 20%
Nutrition funding: None

Project description:

A survey will be conducted among populations at different risks of colon cancer to determine the degree of neutral sterol (cholesterol and coprostanol) degradation. An attempt will be made to isolate intestinal microorganisms responsible for the reduction of neutral sterols. Metabolic pathways of neutral sterol degradation will be studied. The relationship between the physical state of neutral sterols and availability for reduction by intestinal microorganisms will be investigated.

Identifying number: N01 CP 55702
Principal investigator: Franz Halberg
Institution: University of Minnesota, St. Paul
Title: Rhythmometry of Female Volunteers of Different Ages

Total FY79 obligation: $62,010
Nutrition allotment: 10%
Nutrition funding: $6,201

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Project description:

Populations of American and Japanese women will be placed on a protocol specifically designed to assess the levels of a variety of hormones in the blood at various times of the day and month. The goal is to assess the circadian or ultradian rhythms associated with these hormone levels within the two populations and to relate these to other cyclic patterns of sleep, food consumption, menstruation, heartbeat, and blood pressure.

Identifying number: N01 CM 57035
Principal investigator: Emil Frei III
Institution: Sidney Farber Cancer Institute
Title: Therapy of Patients With Large Bowel Carcinoma

Total FY79 obligation: $70,266
Nutrition allotment: 10%
Nutrition funding: $7,027

Total FY80 obligation: Active, not funded
Nutrition allotment: 10%
Nutrition funding: None

Project description:

Patients with large bowel cancer will be studied. Protocols specify nutritional assessment, i.e., caloric intake and nutritional support. Nutritional status will be studied with the use of body weight as a prognostic indicator.

Identifying number: N01 CM 57042
Principal investigator: Gerald P. Bodey
Institution: University of Texas System Cancer Center, M.D. Anderson
Title: Studies of Patients With Solid Disseminated Tumors

Total FY79 obligation: $254,808
Nutrition allotment: 20%
Nutrition funding: $50,961

Total FY80 obligation: $85,461
Nutrition allotment: 20%
Nutrition funding: $17,092

Project description:

Randomized studies will be done involving non-small-cell cancers of the lung. The randomization will involve TPN plus cancer therapy in one group of patients versus cancer therapy alone in a control group of patients.

Identifying number: N01 CP 61031
Principal investigator: Ronald Altman
Institution: New Jersey State Department of Health
Title: Etiologic Studies of Cancer in New Jersey

Total FY79 obligation: $499,900
Nutrition allotment: 20%
Nutrition funding: $99,980

Total FY80 obligation: $424,334
Nutrition allotment: 20%
Nutrition funding: $84,866

Project description:

This study is an 18-month project designed principally to provide the Commissioner of Food and Drugs with an answer to the question: Does saccharin initiate or promote human bladder cancer? The study employs a population-based case-control design. All newly diagnosed carcinomas of the urinary bladder occurring during 1978 in five designated states and four metropolitan areas will be studied. It is estimated that there will be approximately 3,200 cases. In addition, 6,400 controls will be drawn as a stratified random sample of the general population.

Identifying number: N01 CP 61034
Principal investigator: Ann Toledo
Institution: Westat Research, Inc.
Title: Support Services for Field Studies

Total FY79 obligation: $880,312
Nutrition allotment: 25%
Nutrition funding: $220,078

Total FY80 obligation: $98,390
Nutrition allotment: 25%
Nutrition funding: $24,598

Project description:

This contract provides the field interview teams for the following in-house research projects:

(1) A case-control study of esophageal cancer is being conducted among black male residents of Washington, D.C. Black men living in the District of Columbia have mortality rates for this tumor which are among the very highest in the United States. These rates are continuing to increase. In contrast, esophageal cancer is still relatively rare among D.C.'s white male residents. This situation is highly suggestive of an environmental influence peculiar to black men of the District. The aim of this epidemiologic investigation is to identify the risk factors which may be responsible for these unusual patterns.

Support Services for Field Studies (continued)

The study involves interviewing recently diagnosed esophageal cancer cases and controls to elicit lifetime histories of alcohol and tobacco consumption, diet, residence, occupation, and information on several other suspected risk factors for this disease. The beverage history and diet history aspects comprise approximately one-third of the questionnaire.

(2) A case-control interview study is being conducted, involving cases of bladder cancer diagnosed over the last 5 years in certain rural areas of Vermont, New Hampshire, and Maine. These areas are unique in having significantly elevated bladder cancer mortality rates for both sexes. The interview will include information on coffee drinking, the use of nonnutritive sweeteners, use of bracken fern in the diet, and detailed information on sources of drinking water.

(3) The Atlas of Cancer Mortality in the United States (1950-1969) has identified Butler and Colfax counties in rural Nebraska as having among the highest mortality rates for colorectal cancer in the country. These areas do not have the usual demographic characteristics associated with colon and rectal cancer cases. Cases will be matched to two hospital-based controls, and the entire cohort will be intensively interviewed to evaluate the possible etiologic roles of diet, ethnicity, occupation (including job-related chemical exposures) and genetic/familial factors in the high frequency of large bowel cancer in this area.

(4) Another study involves interviewing about 1,300 Canadian women as controls for cases already collected in northern Alberta, Canada. The interview will include a section on dietary patterns in order to determine whether there is any relationship between dietary intake and the incidence of breast cancer.

Identifying number: N01 CP 61060
Principal investigator: Abraham M. Nomura
Institution: Kuakini Medical Center
Title: Japan-Hawaii Cancer Study

Total FY79 obligation: $454,440
Nutrition allotment: 100%
Nutrition funding: $454,440

Total FY80 obligation: $569,562
Nutrition allotment: 100%
Nutrition funding: $569,562

Project description:

This is a long-term prospective study of a cohort of over 6,000 Japanese men in Hawaii. They are being monitored primarily for morbidity and mortality from stomach cancer and large bowel cancer. They had a thorough clinical examination and provided a detailed dietary history. Earlier studies have shown that cancer risks for Japanese migrants differ from those observed in Japan. The migrant risks are higher for lung, colon, rectum, and prostate cancer, and lower for stomach cancer. Case-control studies show an excess consumption of salted and dried fish and salt-pickled vegetables, some of which are rich in secondary amines, by stomach cancer patients. Since nitrites and secondary amines can be synthesized in vivo into nitrosamines, which are potent carcinogens, a possible etiology is suggested for further study.

Case-control studies of Hawaiian Japanese have revealed excess risks of large bowel cancer for persons who regularly ate Western-style meals only. Large bowel cancer was associated with consumption of meats, legumes, and legume effects, and the case-control contrasts were strengthened when various combinations of foods were considered. These findings have stimulated the search for etiologic factors, and the studies in Hawaii and Japan are now involved in a search for differences in intestinal flora and fecal chemistry between the native and migrant Japanese. With the development of bacterial mutagen assays such as the Ames test, it has become possible to screen fecal samples from large numbers of people for the presence of mutagens.

Identifying number: N01 CO 65329
Principal investigator: Karen M. Levin
Institution: Biospherics, Inc.
Title: Information Services for Cancer-Related Inquiries

Total FY79 obligation: $286,789
Nutrition allotment: 5%
Nutrition funding: $14,339

Total FY80 obligation: N/A Terminated

Project description:

Information services will be maintained to provide a response to cancer-related inquiries. Certain public inquiries concerning nutrition and cancer are handled through this contract.

Identifying number: N01 CP 65759
Principal investigator: Jack Fensterstock
Institution: Enviro Control, Inc.
Title: Services to the Diet, Nutrition and Cancer Program

Total FY79 obligation: $676,750
Nutrition allotment: 100%
Nutrition funding: $676,750

Total FY80 obligation: N/A Terminated

Project description:

Assistance will be provided in the development of a diet and nutrition program based on data furnished by the Advisory Committee. Arrangements will be made to obtain data for publications, contract reports, etc., and to maintain and enforce administrative calendars of all diet and nutrition activities as follows: organize and coordinate meetings and develop agendas; determine attendees and arrange travel and lodging; ensure receipt of all material and distribution; attend all meetings; and arrange for recording, transcription, and printing for meetings as required. Liaison will be maintained with approximately 15 members of the Diet, Nutrition and Cancer Program Advisory Committee; diet and nutrition and cancer research contractors; project officers and staff members; NCI contracting officer as necessary; and DNCP consultants as directed. Support will be provided to the project officer (e.g., literature searches, abstracts of scientific articles) for technical studies, definitions of new projects, and definition of performance standards.

Identifying number: N01 CP 65779
Principal investigator: W. DeWys
Institution: Northwestern University
Title: Anorexia in Adult and Pediatric Cancer Patients

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The purpose of this study is to document the existence or nonexistence of weight loss in different groups of cancer patients and to form hypotheses on the possible causes, especially the problem of decreased nutrient intake. A retrospective study of past patient records is being undertaken to determine what percentage of cancer patients have nutritional problems, whether these problems are associated with tumor type and/or treatment, and when in the disease course the nutritional problems develop. Patients are also being monitored prospectively to see if nutritional problems can be primarily ascribed to decreased eating, metabolic changes, biochemical parameters, or other factors. In patients whose nutritional problems seem to be due to decreased eating, therapy, taste and smell changes, food preference changes, psychosocial problems, and other patient characteristics will be observed for the purpose of forming hypotheses to be investigated in future studies. Methodologies will be developed to minimize effects of cancer therapy, increase survival ratio, prolong survival times, and improve overall quality of life.

Identifying number: N01 CP 65786
Principal investigator: James Robertson
Institution: University of Tennessee
Title: Differential Nutritional Requirements of Host and Tumor

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The objective of this project is to evaluate the hypothesis that effective treatment of patients with malignant brain tumors can be undertaken by controlling the blood levels of the specific amino acids required by that particular tumor. In addition, this study seeks to determine 1) whether direct nutritional therapy and concomitant antineoplastic therapy results in synergistic benefits and 2) how direct nutritional therapy affects the host-tumor response and other associated parameters such as host-immune response.

Identifying number: N01 CP 65787
Principal investigator: Sophia S. Fotopoulos
Institution: Midwest Research Institute
Title: Application of Behavior Modification Techniques in the
Treatment of Anorexia in Cancer Patients

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Application of Behavior Modification Techniques in the Treatment of Anorexia in Cancer Patients (continued)

Total FY80 obligation: N/A Terminated

Project description:

The object of this project is to develop behavior modification techniques and evaluate their effectiveness in improving the caloric and nutrient intake of both pediatric and adult cancer patients.

Identifying number: N01 CP 65788
Principal investigator: Seymour L. Romney
Institution: Yeshiva University, New York
Title: Correlation of Epidemiologic and Metabolic Parameters

Total FY79 obligation: $25,000
Nutrition allotment: 100%
Nutrition funding: $25,000

Total FY80 obligation: $73,500
Nutrition allotment: 100%
Nutrition funding: $73,500

Project description:

This project will be coordinated with other DNCP projects in epidemiology and also with associated clinical and laboratory investigations. These studies will be oriented to further defining known or suspected dietary links to cancer through correlation of body pools of specific compounds and dietary intake with the incidence of carcinogenesis. Data will be collected on dietary and nutrient intake and associated metabolic information for "at risk" population groups. The contractor may be required to provide various biological samples and specimens for possible collaborative analysis by other researchers.

Identifying number: N01 CP 65790
Principal investigator: Ilene L. Bernstein
Institution: Children's Orthopedic Hospital and Medical Center
Title: Evaluation of the Role of Learned Food Aversion
in the Cancer Patient

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project will determine whether learned taste aversions are acquired by patients treated with therapeutic regimes that induce gastrointestinal toxicity. The study will include both laboratory and clinical experiments involving patients receiving chemotherapy. Positive results, indicating the development of such aversions, is being followed up with evaluations of their contribution to the anorexia frequently afflicting cancer patients.

Identifying number: N01 CP 65791
Principal investigator: Morley Kare
Institution: University of Pennsylvania
Title: Taste Evaluation of Cancer Patients

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project, which involves multi-institutional therapeutic research, consists of a gustatory evaluation of cancer patients to determine whether significant changes in taste perception occur with tumor type, tumor stage, or treatment modalities. The tumor types include gastrointestinal, mammary, pulmonary, gynecological/urinary, and hematologic classifications. The tumor stages are defined as early and advanced. Treatment modalities include chemotherapy, radiotherapy, and surgery. Changes in recognition threshold and taste preference for the four primary senses of taste (sweet, salt, sour, and bitter) are being examined in cancer patients and in matched controls.

Identifying number: N01 CP 65794
Principal investigator: Jan Van Eys
Institution: University of Texas System Cancer Center, Houston
Title: Optimal Nutritional Support as Adjunct to Cancer Therapy

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Optimal Nutritional Support as Adjunct to Cancer Therapy (continued)

Project description:

This is a multidisciplinary project coordinated with other DNCP projects in the clinical field to determine 1) whether optimal nutritional support alters the rate of tumor growth; 2) whether optimal nutritional support alters the status of the pediatric cancer patient such that the patient's tolerance to antineoplastic therapy and the efficacy of therapy are increased; 3) whether specific antineoplastic therapy interferes with the efficacy of nutritional therapy, impairs utilization, or causes complications; and 4) how optimal nutritional support affects the host-tumor response and host-immune response to cancer therapy.

Identifying number: N01 CP 65802
Principal investigator: James Mullen
Institution: University of Pennsylvania
Title: Optimal Nutritional Support as Adjunct to Cancer Therapy

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This is a multidisciplinary project coordinated with other DNCP efforts in the clinical field. This project will determine whether optimal nutritional support alters the rate of tumor growth and alters the status of the adult cancer patient such that the patient's tolerance to antineoplastic therapy is increased and the efficacy of therapy is increased.

Identifying number: N01 CP 65818
Principal investigator: Ernst L. Wynder
Institution: American Health Foundation, New York
Title: Correlation of Epidemiologic and Metabolic Parameters

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project will be coordinated with other DNCP activities in epidemiology and also with associated clinical and laboratory investigations. These studies will be oriented to further defining known or suspected dietary links to cancer through correlation of body pools of specific compounds and dietary intake with the incidence of carcinogenesis. Data will be collected on dietary and nutrient intake and associated metabolic information for "at risk" population groups. Biological samples and specimens will be provided on request for possible collaborative analysis by other researchers.

Identifying number: N01 CP 65834
Principal investigator: Giovanni G. Costa
Institution: State University of New York, Buffalo
Title: Anorexia in Adult and Pediatric Cancer Patients

Total FY79 obligation: $50,000
Nutrition allotment: 100%
Nutrition funding: $50,000

Total FY80 obligation: N/A Terminated

Project description:

The purpose of this study is to document the existence or nonexistence of weight loss in different groups of cancer patients and to form hypotheses on the possible causes, especially the problem of decreased nutrient intake. A retrospective study of past patient records is being undertaken to determine what percentage of cancer patients have nutritional problems, whether these problems are associated with tumor type and/or treatment, and when in the disease course the nutritional problems develop.

Patients are also being monitored prospectively to see if nutritional problems can be primarily ascribed to decreased food intake, metabolic changes, biochemical parameters, or other factors. Patients whose nutritional problems seem to be due to decreased food intake, therapy, taste and smell changes, food preference changes, psychosocial problems, and other patient characteristics will be observed for the purpose of forming hypotheses to be investigated in future studies. Methodologies will be developed to minimize effects of cancer therapy, increase survival ratio, prolong survival times, and improve overall quality of life.

Identifying number: N01 CP 65836
Principal investigator: Robert Henkin
Institution: Georgetown University
Title: Anorexia in Adult and Pediatric Cancer Patients

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The purpose of this study is to document the existence or nonexistence of weight loss in different groups of cancer patients and to form hypotheses on the possible causes, especially the problem of decreased nutrient intake. A retrospective study of past patient records is being undertaken to determine what percentage of cancer patients have nutritional problems, whether these problems are associated with tumor type and/or treatment, and when in the disease course the nutritional problems develop.

Patients are also being followed prospectively to see if nutritional problems can be primarily ascribed to decreased eating, metabolic changes, biochemical parameters, or other factors. In patients whose nutritional problems seem to be due to decreased eating, therapy, taste and smell changes, food preference changes, psychosocial problems, and other patient characteristics will be observed for the purpose of forming hypotheses to be investigated in future studies. Methodologies will be developed to minimize effects of cancer therapy, increase survival ratio, prolong survival times, and improve overall quality of life.

Identifying number: N01 CP 65866
Principal investigator: Melvin L. Samuels
Institution: M.D. Anderson Hospital and Tumor Institute
Title: Optimal Nutritional Support as Adjunct to Cancer
Therapy in the Adult Patient

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: $5,500
Nutrition allotment: 100%
Nutrition funding: $5,500

Project description:

This multi-institutional study is examining optimal nutritional support, specifically total parenteral nutrition of adult patients with testicular carcinoma, to determine its effects on tumor growth, tolerance to antineoplastic therapy, and host-tumor response and to evaluate its safety, efficacy in maintaining the nutritional status of cancer patients, and usefulness in improving quality of life. All patients studied are on active cancer therapy programs, including surgery, radiotherapy, and chemotherapy. The protocol also requires the collection of red blood cells and plasma samples from patients at data collection points. These samples will be stored until the completion of patient entry at which time decisions will be made on the components to be quantitated. Patient entry into this study stopped June 30, 1978. Preliminary analysis of data collected during the active phase of the study is being conducted.

Identifying number: N01 CP 65867
Principal investigator: Kumao Sako
Institution: Roswell Park Memorial Institute
Title: Optimal Nutritional Support as Adjunct to Cancer
Therapy in the Adult Patient

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This multi-institutional study is examining optimal nutritional support, specifically, total parenteral nutrition of adult patients with head and neck malignancies, to determine its effect on tumor growth, tolerance to antineoplastic therapy, and host-tumor response and to evaluate its safety, efficacy in maintaining the nutritional status of cancer patients, and usefulness in improving quality of life. All patients studied are on active cancer therapy programs, including surgery, radiotherapy, and chemotherapy. The protocol also requires the collection of red blood cells and plasma samples from patients at data collection points. These samples will be stored until the completion of patient entry at which time decisions will be made on the components to be quantitated. Patient entry into this study stopped June 30, 1978. Preliminary analysis of data collected during the active phase of the study is being conducted.

Identifying number: N01 CP 65868
Principal investigator: John M. Love
Institution: State University of New York, Buffalo
Title: Optimal Nutritional Support as Adjunct to
Cancer Therapy in the Adult

Total FY79 obligation: $33,876
Nutrition allotment: 100%
Nutrition funding: $33,876

Total FY80 obligation: N/A Terminated

Project description:

This multi-institutional study is examining optimal nutritional support, specifically, total parenteral nutrition of adult patients with squamous cell carcinoma of the head and neck, to determine its effects on tumor growth, tolerance to antineoplastic therapy, and host-tumor response and to evaluate its safety, efficacy in maintaining the nutritional status of cancer patients, and usefulness in improving quality of life. All patients studied are on active cancer therapy programs, including surgery, radiotherapy, and chemotherapy. The protocol also requires the collection of red blood cells and plasma samples from patients at data collection points. These samples will be stored until the completion of patient entry at which time decisions will be made on the components to be quantitated. Patient entry into this study stopped June 30, 1978. Preliminary analysis of data collected during the active phase of the study is being conducted.

Identifying number: N01 CP 65869
Principal investigator: William P. Steffee
Institution: University Hospital, Boston
Title: Optimal Nutritional Support as Adjunct to Cancer Therapy

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The objective of this work is to determine 1) whether optimal nutritional support alters the rate of tumor growth; 2) whether optimal nutritional support alters the status of the adult cancer patients such that the patient's tolerance to antineoplastic therapy is increased and the efficacy of therapy is increased; 3) whether specific antineoplastic therapy interferes with the efficacy of nutritional therapy, impairs utilization or causes complications; and 4) how optimal nutritional support affects the host-tumor response and host-immune response to cancer therapy.

Identifying number: N01 CP 65870
Principal investigator: George L. Blackburn
Institution: New England Deaconess Hospital
Title: Optimal Nutritional Support as Adjunct to Cancer Therapy in the Adult Patient

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The purpose of this project is to study specific total parenteral nutrition techniques in adult breast cancer patients. Patients will be monitored during and after the experimental period to assess their response to therapy and nutritional supplementation.

Identifying number: N01 CP 65871
Principal investigator: Victor J. Lanzotti
Institution: M.D. Anderson Hospital
Title: Optimal Nutritional Support as Adjunct to Cancer Therapy in the Adult Patient

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project will be a multidisciplinary project coordinated with other DNCP projects to determine 1) whether optimal nutritional support alters the rate of tumor growth; 2) whether optimal nutritional support alters the status of the adult cancer patient such that the patient's tolerance to antineoplastic therapy is increased and the efficacy of

Optimal Nutritional Support as Adjunct to Cancer Therapy in the Adult Patient (continued)

therapy is increased; 3) whether specific antineoplastic therapy interferes with the efficacy of nutritional therapy, impairs utilization or causes complications; and 4) how optimal nutritional support affects the host-tumor response and host-immune response to cancer therapy.

Each research institution will be responsible for conducting, under a common protocol, a study of non-oat cell carcinoma of the lung in adult cancer patients being treated by chemotherapy. Patients will be assigned to nutritional regimes involving the use of specific total parenteral nutrition techniques. During and after the experimental period, patients will be monitored and evaluated to assess their response to therapy and nutritional support.

Identifying number: N01 CP 65873
Principal investigator: Daniel W. Nixon
Institution: Emory University School of Medicine
Title: Optimal Nutritional Support as Adjunct to Cancer Therapy in the Adult Patient

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This multi-institutional study is examining optimal nutritional support, specifically total parenteral nutrition of adult patients with adenocarcinoma of the colon, to determine its effects on tumor growth, tolerance to antineoplastic therapy, and host-tumor response and to evaluate its safety, efficacy in maintaining the nutritional status of cancer patients, and usefulness in improving quality of life. All patients studied are on active cancer therapy programs, including surgery, radiotherapy, and chemotherapy. The protocol also requires the collection of red blood cells and plasma samples from patients at data collection points. These samples will be stored until the completion of patient entry, at which time decisions will be made on the components to be quantitated. Patient entry into this study stopped June 30, 1978. Preliminary analysis of data collected during the active phase of the study is being conducted.

Identifying number: N01 CM 67110
Principal investigator: Phillip S. Schein
Institution: Georgetown University
Title: Gastrointestinal Cancer Research Program

Total FY79 obligation: $52,030
Nutrition allotment: 20%
Nutrition funding: $10,406

Total FY80 obligation: Active, not funded
Nutrition allotment: 20%
Nutrition funding: None

Project description:

Studies will be done on the diagnosis and treatment of gastrointestinal cancers. One study will examine the effects of chemotherapy on intestinal function to determine if cancer patients receiving chemotherapy develop malabsorption. Another study will examine the glucose tolerance of cancer patients to explore the potential role of insulin ineffectiveness in the cachexia syndrome.

Identifying number: N01 CP 71005
Principal investigator: Patricia Buffler
Institution: University of Texas Medical Branch
Title: Epidemiology of Primary Liver Cancer in Selected Counties of Texas

Total FY79 obligation: Active, not funded
Nutrition allotment: 20%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This project is designed to study mortality from primary liver cancer in selected counties in Texas. These counties were selected because they have the highest rates of primary liver cancer in this country. Utilizing a case-control approach for this investigation, characteristics of the patients, such as employment in the chemical industry, are compared to persons free of the disease. A component of this study is planned with emphasis on nutrition in Rio Grande Valley. This component will characterize the diet of residents in this region with regard to ingestion of mycotoxins.

Identifying number: N01 CP 71048
Principal investigator: Janez Knut/N.E. Day
Institution: World Health Organization International Agency for Research on Cancer, Lyon, France
Title: Etiology of Esophageal Cancer in Iran

Total FY79 obligation: $14,154
Nutrition allotment: 100%
Nutrition funding: $14,154

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

In a study of cancer of the esophagus in Iran, scientists are examining the relationship of incidence of this cancer with various factors such as heredity, immune response, opium use, food (mostly wheat), and wheat contaminants. In the nutrition portion of this study an extensive nutritional and food consumption survey was conducted in 38 villages in the Caspian Littoral of Iran. The eastern regions of this area are characterized by high incidence of esophageal cancer, the western regions by lower incidence. Besides showing differences between the diets of the populations in the eastern and western regions, the survey found that in the high incidence regions there was a low intake of vitamins A and C and riboflavin.

In a more detailed followup nutrition survey of a smaller sampling of villages, investigators found substantial riboflavin deficiency throughout all the locations. This finding indicates that, if riboflavin deficiency has a role to play in cancer of the esophagus, it is probably that of facilitating an unknown carcinogen (possibly in the opium products used) by somehow impairing the immune system.

Preliminary results of a case-control study suggest that the risk of developing cancer of the esophagus is linked to a low socioeconomic status and the consumption of a restricted diet.

The Iranians being monitored in this study are Moslems and, according to their religion, alcohol is proscribed. There is no evidence that alcohol plays any part in cancer of the esophagus in Iran. Dietary deficiencies interacting with alcohol and tobacco have been suggested as a possible basis for high rates of cancer of the esophagus in blacks in the United States.

Identifying number: N01 CB 74102
Principal investigator: Baruch Modan
Institution: Chaim Sheba Medical Center, Tel Hashomer, Israel
Title: Epidemiology of Benign Breast Disease

Total FY79 obligation: $90,995
Nutrition allotment: 60%
Nutrition funding: $54,597

Total FY80 obligation: $48,963
Nutrition allotment: 60%
Nutrition funding: $29,377

Project description:

The object of this study is to determine the characteristics of patients with different types of noninvasive breast lesions, with particular reference to those factors reputed to be preferentially associated with breast cancer, and to compare the findings with a similarly conducted breast cancer study.

The project consists of two phases: a case-control interview study of 600 cases of noninvasive breast disease, and an incidence study of noninvasive breast lesions in a total community. In both phases, particular attention is paid to the relative frequency of distinct histopathological forms in high- and low-risk subpopulations for breast cancer, i.e., European vs. Asian and African born. The characterization of the breast lesions will take into account the histological pattern, degree of atypia, and lymphoreticuloendothelial response.

Identifying number: N01 CB 74104
Principal investigator: Sherwood L. Gorbach
Institution: New England Medical Center
Title: Relation of Intestinal Flora to Breast Cancer in Humans

Total FY79 obligation: $105,000
Nutrition allotment: 25%
Nutrition funding: $26,250

Total FY80 obligation: $21,800
Nutrition allotment: 25%
Nutrition funding: $5,450

Project description:

This study is to determine the role of the intestinal microflora in the metabolism of biologically significant estrogens in women who are at high and low risk for breast cancer.

Identifying number: N01 CB 74188
Principal investigator: Gordon H. Sato
Institution: University of California, La Jolla
Title: Growth and Passage of Mammary Epithelial Cells in Culture

Total FY79 obligation: $65,300
Nutrition allotment: 50%
Nutrition funding: $32,650

Total FY80 obligation: $71,500
Nutrition allotment: 50%
Nutrition funding: $35,750

Project description:

The objective of this project is to determine the hormonal and nutritional requirements of established animal and human mammary tumor cell lines and to isolate and maintain growth of pure mammary epithelial cells in culture.

Identifying number: N01 CB 74207
Principal investigator: Richard C. Moon
Institution: IIT Research Institute
Title: Prevention of Preneoplastic Lesions of the Mammary Gland

Total FY79 obligation: $90,300
Nutrition allotment: 50%
Nutrition funding: $45,150

Total FY80 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Project description:

The purpose of this project is to prevent the development and/or progression of preneoplastic lesions of the mammary gland of experimental animals. The approach involves pharmacological intervention in the process of cellular differentiation through the administration of nontoxic doses of synthetic analogs of vitamin A.

Identifying number: N01 CO 75351
Principal investigator: Robert M. Kelley/Carol Hart
Institution: Kappa Systems, Arlington, Virginia
Title: National Cancer Program Information Clearinghouse

Total FY79 obligation: $308,043
Nutrition allotment: 5%
Nutrition funding: $15,402

Total FY80 obligation: $89,949
Nutrition allotment: 5%
Nutrition funding: $4,497

Project description:

This project encompasses various information support services for NCI's public information and public education activities, patient education, and certain limited areas of professional information (dissemination and information referral) services. Performance of this contract involves cataloging materials, operating storage and retrieval systems, and assisting in the development of public information and educational products and services including materials on diet, nutrition, and cancer.

Identifying number: N01 CO 75380
Principal investigator: Michael G. Hanna
Institution: Litton Bionetics, Inc.
Title: Operation of the Frederick Cancer Research Center

Total FY79 obligation: $29,148,015
Nutrition allotment: 1%
Nutrition funding: $291,480

Total FY80 obligation: $31,983,709
Nutrition allotment: 1%
Nutrition funding: $319,837

Project description:

The management, operation, and maintenance of the Frederick Cancer Research Center will be provided by Litton Bionetics, Inc., for the National Cancer Institute. Research studies and investigations encompass a broad spectrum of cancer research, both basic and applied, involving several program areas such as viral oncology, chemical carcinogenesis, basic research, animal holding, breeding and diagnostic procedures, biohazard and environmental control, cancer treatment, and special histopathology, plus NINCDS support.

Identifying number: N01 CP 75881
Principal investigator: William Banks
Institution: Virginia Commonwealth University, Richmond
Title: Differential Nutritional Requirements in Treatment of Brain Tumors

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The objective of this project is to evaluate the hypothesis that effective treatment of patients with malignant brain tumors can be achieved by controlling the blood levels of the specific amino acids required by the particular tumor. In addition, this study seeks to determine 1) whether direct nutritional therapy and concomitant antineoplastic therapy results in synergistic benefits; and 2) how direct nutritional therapy affects the host-tumor response and other associated parameters such as host-immune response.

Identifying number: N01 CP 75897
Principal investigator: Koji Nakanishi
Institution: Columbia University
Title: Synthesis of New Retinoids

Total FY79 obligation: $83,572
Nutrition allotment: 100%
Nutrition funding: $83,572

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The goal of this project is to synthesize retinoids for in vitro studies. The approach will involve the synthesis of small quantities of different retinoids, the choice of which will be dictated by the needs and interests of the NCI Carcinogenesis Program. In general, the following services will be provided: a synthesis of a variety of retinoids with different side chains and/or ring structures; a synthesis of a variety of radioactive retinoids, depending on NCI needs; purified compounds suitable for testing; data documenting the radiochemical and chemical purity of each compound; and a small sample of the compound for verification of purity.

Identifying number: N01 CP 75899
Principal investigator: Willard J. Visek
Institution: University of Illinois
Title: Effect of Dietary Protein on Carcinogenesis

Total FY79 obligation: $482,000
Nutrition allotment: 100%
Nutrition funding: $482,000

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The objective of this project is to evaluate the effects of types of protein and level of protein on the induction and progression of spontaneous and chemically induced tumors in laboratory animals. The experiment will be a factorially designed study of 30 experimental treatments (2 protein sources x 3 dietary levels x 5 carcinogens) plus 6 control treatments (2 protein sources x 3 dietary levels) for the observation of spontaneous tumors. The American Institute of Nutrition standard diet for mice will be used as the reference diet in this study. The protein sources will be semipurified casein and isolated soy protein. Each will be fed at 10, 20, and 40 percent of the diet.

The carcinogens will be selected to represent each of the five major classes of carcinogens: polycyclic hydrocarbons, aromatic amines, alkylating agents, nitrosamines, and naturally occurring carcinogens. The carcinogens will be administered orally at low doses throughout the experiment. Prior to initiation of the chronic study, the dose level of carcinogens will be based on absorption and metabolic characteristics of the carcinogens. Each experimental diet-carcinogen combination will be fed to 25 male and 25 female mice for 24 months.

Identifying number: N01 CP 75905
Principal investigator: William Croft
Institution: University of Wisconsin
Title: Prevention of Epithelial Cancer by Retinoids

Total FY79 obligation: $146,000
Nutrition allotment: 100%
Nutrition funding: $146,000

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The goal of this project is to determine the efficacy of a number of retinoids of differing chemical structure in preventing development of bladder cancer during its preneoplastic stage. The FANFT mode is used for induction of bladder cancer. The effects of retinoids on the bladder and on tumor development will be studied by observation of bladder weight; number of tumors per bladder detected grossly; percent of bladder having hyperplasia, papilloma, and carcinomas (staging of urinary bladder pathology will be based on the World Health Organization); and recording of other pathological lesions, including other tumors. FANFT will be monitored in the feed or ANFT in the urine by quantitation of Salmonella typhimurium revertants produced by urine of experimental animals. Blood and tissue levels of retinoids will be monitored in experimental animals.

Identifying number: N01 CP 75911
Principal investigator: Hans H. Kaegi
Institution: Midwest Research Institute
Title: Synthesis of Radioactive Retinoids

Total FY79 obligation: $203,042
Nutrition allotment: 100%
Nutrition funding: $203,042

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to synthesize, isolate, purify, analyze, and supply small quantities of NCI-selected radioactive retinoids for use as tracers in metabolic studies, both in vivo and in vitro.

Specifically, from 5 to 50 mCi of each radiolabeled material will be produced at specific activities of 1 or 2 Ci/mmole (^3H) and 10 to 100 mCi/mmole (^{14}C), depending on NCI needs and methods of preparation; compounds will be furnished to the NCI Carcinogenesis Program which will be directly suitable for research proposed without further purification.

Data documenting the radiochemical and chemical purity of each product will be supplied prior to shipment along with a small sample of the radioactive compound.

Identifying number: N01 CP 75915
Principal investigator: Hiromu Matsumoto
Institution: University of Hawaii, Manoa
Title: Cycasin and Macrozamin as Potential Carcinogens

Total FY79 obligation: $83,221
Nutrition allotment: 100%
Nutrition funding: $83,221

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

Support to be provided will include services, qualified personnel, material, and facilities not otherwise provided by the government as needed to develop a routine assay procedure for the presence of the methylazoxymethanol glycosides (cycasin and macrozamin), methylazoxymethanol and methylazoxymethanol glucuronide in meat samples; to determine the limits of detection, sensitivity, and reproducibility of the analytical system; to add known amounts of methylazoxymethanol, its glycosides and glucuronide to meat and determine the percentage of recovery; and to determine the effects of storage and heating to temperatures ordinarily used in cooking on the recovery of known amounts of methylazoxymethanol, its glycosides, and its glucuronides from meat samples.

Identifying number: N01 CP 75931
Principal investigator: Marcia I. Dawson
Institution: SRI International
Title: Synthesis of New Retinoids

Total FY79 obligation: $149,736
Nutrition allotment: 100%
Nutrition funding: $149,736

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to synthesize several retinoids with better pharmacological properties than those that have already been tested. The approach will involve the synthesis of several different retinoids, the choice of which will be dictated by NCI Carcinogenesis Program. In general, this project will synthesize, purify, and characterize a variety of retinoids; conduct a systematic structure-activity relationship; synthesize analogs of vitamin A with both steric and electronic modifications in the ring, the side chain, and the polar terminals; prepare retinoids with potential organ specificity; correlate the activity of several substituted phenyl retinoids with the values of three substituents; and supply the synthetic retinoids in the purest possible form to NCI for in vitro biological evaluations. Data documenting the chemical purity of each compound will be supplied along with a small sample of the compound.

Identifying number: N01 CP 75932
Principal investigator: F. I. Carroll
Institution: Research Triangle Institute
Title: Synthesis of New Retinoids

Total FY79 obligation: $125,510
Nutrition allotment: 100%
Nutrition funding: $125,510

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to synthesize small quanitites of retinoids to investigate the effects of structure modification on effectiveness of retinoids in controlling differentiation of epithelial tissue in vitro. The approach will involve the synthesis of small quantities of a variety of retinoids, the choice of which will be specified by NCI.

In general, this project will synthesize four classes of retinoids (derivatives of 13-cis retinoids, cyclic derivatives of all-trans retinoids, all-trans retinoids substituted in the polyene side chain, and analogs of retinyl amine); present complete physical and chemical data including UV, IR, NMR spectra, analyses for carbon, hydrogen and other elements, and determination of purity by HPLC or TLC or special group analyses when indicated; and provide information regarding the solubility and stability of the prepared samples in aqueous media at neutral pH.

Identifying number: N01 CP 75933
Principal investigator: Robert S. Liu
Institution: University of Hawaii, Manoa
Title: Synthesis of New Retinoids

Total FY79 obligation: $42,847
Nutrition allotment: 100%
Nutrition funding: $42,847

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to synthesize, purify, analyze, and supply NCI with sufficient quantities of retinoids for chemoprevention and toxicity studies. The approach will involve the synthesis of quantities of modified retinoids, the choice of which will be dictated by NCI. In general, this project will synthesize a variety of geometric isomers of retinoids; provide assay and analytical data on all compounds; supply 100 mg of each purified compound; and prepare data sheets describing preparative methods and requirements for handling and storing materials.

Identifying number: N01 CP 75934
Principal investigator: Clayton H. Heathcock
Institution: University of California, Berkeley
Title: Synthesis of New Retinoids

Total FY79 obligation: $55,166
Nutrition allotment: 100%
Nutrition funding: $55,166

Synthesis of New Retinoids (continued)

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project will provide synthesis of new retinoids for in vitro studies. The approach involves the synthesis of small quantities of several different retinoids, the choice of which will be dictated by the needs and interests of NCI. In general, this project will synthesize a variety of retinoid lactones and esters of retinoic acid; prepare a variety of retinoid analogs that might be metabolized more rapidly; establish the stability of retinoid analogs; forward the synthetic compounds to NCI for biological evaluations; and supply data documenting the chemical purity of each compound and a small sample of the compound.

Identifying number: N01 CP 75935
Principal investigator: Steven C. Welch
Institution: University of Houston
Title: Synthesis of New Retinoids

Total FY79 obligation: $68,113
Nutrition allotment: 100%
Nutrition funding: $68,113

Total FY80 obligation: $1,172
Nutrition allotment: 100%
Nutrition funding: $1,172

Project description:

Retinoids will be synthesized for in vitro studies. The approach will involve the synthesis of several different retinoids, the choice of which will be dictated by the needs and interests of NCI. In general, this project will synthesize a variety of active metabolites of retinoic acid; prepare some selected retinoic acid analogs by isosteric substitution; synthesize the amino acid and glyceride molecular modifications of retinoic acid; submit all retinoids and synthetic retinoic acids to NCI for biological evaluation; and supply data documenting the chemical purity of each compound and a small sample.

Identifying number: N01 CP 75936
Principal investigator: Joseph I. De Graw
Institution: SRI International
Title: Synthesis of Radioactive Retinoids

Total FY79 obligation: $165,484
Nutrition allotment: 100%
Nutrition funding: $165,484

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

Radioactive retinoids will be synthesized for use as tracers in both in vivo and in vitro metabolic studies. The approach will involve the synthesis of small quantities of several different retinoids, the choice of which will be dictated by the needs and interests of NCI. In general, services provided will include synthesis of a variety of radioactive retinoids; assay and analytical data on all compounds; storage packaging and distribution of all compounds; maintenance of an accurate inventory of compounds; and provision of sheets describing preparative methods and requirements for handling and storing materials.

Identifying number: N01 CP 75937
Principal investigator: David G. Ahern
Institution: New England Nuclear Corporation
Title: Synthesis of Radioactive Retinoids

Total FY79 obligation: $197,983
Nutrition allotment: 100%
Nutrition funding: $197,983

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

Radioactive retinoids will be synthesized for use as tracers in metabolic studies, both in vivo and in vitro. The approach will involve the synthesis of small quantities of several different retinoids, the choice of which will be dictated by the needs and interests of the NCI Carcinogenesis Program. In general, this project will synthesize a variety of radioactive retinoids; provide assay and analytical data on all compounds; and prepare data sheets describing methods of preparation and requirements for handling and storing materials.

Identifying number: N01 CP 75938
Principal investigator: R. Marian Hicks
Institution: University of London
Title: Prevention of Epithelial Cancer by Retinoids

Total FY79 obligation: $86,710
Nutrition allotment: 100%
Nutrition funding: $86,710

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

Long-term feeding studies will be done with different retinoids to identify the optimum analog in terms of maximum anticancer activity coupled with minimum toxicity to the animal. Sequential sampling will be done of normal and carcinogen-treated animals maintained on retinoid-containing diets to investigate subcellular changes associated with the anticarcinogenic effect. Determination will be made of whether the retinoid prevents the subsequent growth of initiated cells in the tumors by actually reversing the initiating event, or only delays the appearance of tumors by increasing the latent period before neoplastic growth starts. The minimum time retinoids must act on an initiated urothelium before their anticarcinogenic effect has become irreversible will be determined.

Identifying number: N01 CP 75939
Principal investigator: Richard C. Moon
Institution: IIT Research Institute
Title: Prevention of Epithelial Cancer by Retinoids

Total FY79 obligation: $128,235
Nutrition allotment: 100%
Nutrition funding: $128,235

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The aim of this project is to investigate and ascertain which retinoids are highly effective in inhibiting mammary carcinogenesis induced by N-nitrosomethylurea. It is planned to determine the time that can elapse between the carcinogenic insult and initiation of retinoid treatment without impairment of the efficacy of the retinoid in inhibition of mammary carcinogenesis.

The following parameters will be evaluated in assessing the anticarcinogenic activity of each retinoid studied: percent incidence of mammary cancer and benign cancer and benign mammary tumors; number of mammary cancers and benign tumors; number of invasive tumors; number of mitotic figures; and latent period of tumor appearance. Experimental animals will be observed daily for evidence of retinoid toxicity. All retinoids tested will be studied for evidence of toxicity with the use of liver function and histological measures. The periodicity of the estrous cycle will be established by vaginal smears of rats in the groups. Serum levels of retinoids will be determined on a bimonthly basis for each retinoid investigated.

Identifying number: N01 CP 75940
Principal investigator: John H. Weisburger
Institution: American Health Foundation
Title: Prevention of Epithelial Cancer by Retinoids

Total FY79 obligation: $160,046
Nutrition allotment: 100%
Nutrition funding: $160,046

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The efficacy of retinoids of differing chemical structures to prevent the development of colon cancer during its preneoplastic period will be evaluated. Through the use of a rat model early lesions of epithelial cancers will be recognized and used to test the efficacy of retinoids in the prevention of preneoplastic lesions. The effect of synthetic retinoids on the induction of colon cancer will be studied with the use of the direct-acting carcinogen N-nitrosourea and the indirect acting carcinogen 1,2-dimethylhydrazine. The time of action and effect of dose will be studied by administering N-nitrosourea and 1,2-dimethylhydrazine either as a single dose (or two doses for N-nitrosourea) or in multiple doses and early lesions of colon cancer will be detected. The effect of retinoids in their modification will be evaluated.

Identifying number: N01 CP 75950
Principal investigator: M. Earl Balis
Institution: Sloan-Kettering Institute for Cancer Research
Title: Studies of Metabolic Capacity in Intestinal Mucosa

Total FY79 obligation: $96,748
Nutrition allotment: 100%
Nutrition funding: $96,748

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to investigate enzymology in colonic systems in controls and carcinogen-treated animals. The enzymes to be studied include ornithine decarboxylase, xanthine oxidase, HPRIase, TdKase, phosphoribosylpyrophosphate synthetase, variants of adenosine deaminase, and adenosylmethionine decarboxylase.

These studies will investigate the influence of cholesterol and bile acids on these activities, assess the influence of high-fat and high-protein diets, investigate effects of inducers and inhibitors under many of the conditions cited above, and study localization and possible variant forms of enzymes in crypt and surface cells with the use of plaining techniques and isoenzyme-specific antibodies.

Identifying number: N01 CP 75951
Principal investigator: Lucy Anderson
Institution: Sloan-Kettering Institute for Cancer Research
Title: Studies of Metabolic Capacity in Intestinal Mucosa

Total FY79 obligation: $198,744
Nutrition allotment: 100%
Nutrition funding: $198,744

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to investigate enzymology in colonic systems in controls and carcinogen-treated animals. The enzymes to be studied include ornithine decarboxylase, xanthine oxidase, HPRIase, TdKase, phosphoribosylpyrophosphate synthetase, variants of adenosine deaminase, and adenosylmethionine decarboxylase.

These studies will investigate the influence of cholesterol and bile acids on these activities, assess the influence of high-fat and high-protein diets, investigate effects of inducers and inhibitors under many of the conditions cited above, and study localization and possible variant forms of enzymes in crypt and surface cells with the use of plaining techniques and isoenzyme-specific antibodies.

Identifying number: N01 CP 81011
Principal investigator: David A. Culp
Institution: University of Iowa
Title: Role of Saccharin in Bladder Cancer

Total FY79 obligation: $20,460
Nutrition allotment: 100%
Nutrition funding: $20,460

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The objective of this project is to provide information on the possible role of saccharin in the development of bladder cancer.

Identifying number: N01 CP 81012
Principal investigator: D. Austin
Institution: California State Department of Health
Title: FDA/NCI Special Study of the Role of Saccharin in Bladder Cancer in the General Population

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This is an 18-month project designed principally to provide the Commissioner of Food and Drugs with an answer to the question: Does saccharin initiate or promote human bladder cancer? The study employs a population-based case-control design. All newly diagnosed carcinomas of the urinary bladder occurring during 1978 in five designated states

FDA/NCI Special Study of the Role of Saccharin in Bladder Cancer in the General Population (continued)

and four metropolitan areas will be studied. It is estimated that there will be approximately 3,200 cases. In addition, 6,400 controls will be drawn as a stratified random sample of the general population.

In addition to saccharin ingestion, other exposures will be assessed: occupation, cigarette smoking, source of drinking water, coffee consumption, and intake of liquids. Assessment of historical and current drinking water quality is being made in cooperation with the Environmental Protection Agency.

Identifying number: N01 CP 81013
Principal investigator: J. W. Sullivan
Institution: Louisiana State University Medical Center, New Orleans
Title: Role of Saccharin in Bladder Cancer

Total FY79 obligation: $65,233
Nutrition allotment: 100%
Nutrition funding: $65,233

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The objectives of this project have been reassessed from bladder cancer in its connection with saccharin to bladder cancer and its relationship to Mississippi River drinking water.

Identifying number: N01 CP 81014
Principal investigator: Margaret A. Child
Institution: Emory University
Title: Role of Saccharin in Bladder Cancer

Total FY79 obligation: $74,491
Nutrition allotment: 100%
Nutrition funding: $74,491

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The objectives of this project have been reassessed from bladder cancer in its connection with saccharin to bladder cancer and its relationship to textile production in the Atlanta region.

Identifying number: N01 CP 81015
Principal investigator: Joseph L. Lyon
Institution: University of Utah, Salt Lake City
Title: Role of Saccharin in Bladder Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The objectives of this project are to provide information on the possible harmful effects resulting from the widespread use of saccharin, specifically regarding bladder cancer.

Identifying number: N01 CP 81016
Principal investigator: C. Key
Institution: University of New Mexico
Title: FDA/NCI Special Study of the Role of Saccharin in Bladder Cancer in the General Population

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

This is an 18-month project designed principally to provide the Commissioner of Food and Drugs with an answer to the question: Does saccharin initiate or promote human bladder cancer? The study employs a population-based case-control design. All newly diagnosed carcinomas of the urinary bladder occurring during 1978 in five designated states and four metropolitan areas will be studied. It is estimated that there will be approximately 3,200 cases. In addition, 6,400 controls will be drawn as a stratified random sample of the general population.

FDA/NCI Special Study of the Role of Saccharin in Bladder Cancer in the General Population (continued)

In addition to saccharin ingestion, other exposures will be assessed: occupation, cigarette smoking, source of drinking water, coffee consumption, and intake of liquids. Assessment of historical and current drinking water quality is being made in cooperation with the Environmental Protection Agency.

Identifying number: N01 CP 81017
Principal investigator: Thomas W. McKenna
Institution: Westat Research, Rockville, Maryland
Title: Role of Saccharin in Bladder Cancer

Total FY79 obligation: $53,680
Nutrition allotment: 100%
Nutrition funding: $53,680

Total FY80 obligation: $278,662
Nutrition allotment: 100%
Nutrition funding: $278,662

Project description:

The objective of this project is to provide information on the possible harmful effects resulting from the widespread use of saccharin, specifically regarding bladder cancer.

Identifying number: N01 CP 81022
Principal investigator: William F. Jarrett
Institution: University of Glasgow
Title: Carcinogens and Papilloma Viruses in Cattle Cancer

Total FY79 obligation: $55,788
Nutrition allotment: 50%
Nutrition funding: $27,644

Total FY80 obligation: Active, not funded
Nutrition allotment: 50%
Nutrition funding: None

Project description:

The purpose of this project is to characterize, compare, and contrast the types of papilloma virus isolated from cattle: bovine cutaneous papilloma virus (BUPV); the classical bovine papovirus; bovine alimentary papilloma virus (BUPV); and bovine udder papilloma virus (BUPV). Alimentary squamous carcinomas found in cattle on bracken-infested farms will be investigated for the presence of papilloma virus genome, a similar study will be done of the adenomas and adenocarcinomas found in the intestine, and experimental models will be set up in which the bracken fern component is replaced in "carcinogen plus virus" experiments by such compounds as azothioprene to gain insight into the nature of the mechanism of interplay of the dietary factor and the virus.

Identifying number: N01 CP 81031
Principal investigator: David B. Thomas
Institution: Fred Hutchinson Cancer Research Center, Seattle
Title: Role of Saccharin in Bladder Cancer

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Project description:

The objectives of this project are to provide information on the possible harmful effects resulting from the widespread use of saccharin, specifically regarding bladder cancer.

Identifying number: N01 CP 81049
Principal investigator: P. Scherr
Institution: Michigan Cancer Foundation
Title: FDA/NCI Special Study of the Role of Saccharin in Bladder
Cancer in the General Population

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

FDA/NCI Special Study of the Role of Saccharin in Bladder Cancer in the General Population (continued)

Project description:

This is an 18-month project designed principally to provide the Commissioner of Food and Drugs with an answer to the question: Does saccharin initiate or promote human bladder cancer? The study employs a population-based case-control design. All newly diagnosed carcinomas of the urinary bladder occurring during 1978 in five designated states and four metropolitan areas will be studied. It is estimated that there will be approximately 3,200 cases. In addition, 6,400 controls will be drawn as a stratified random sample of the general population.

In addition to saccharin ingestion, other exposures will be assessed: occupation, cigarette smoking, source of drinking water, coffee consumption, and intake of liquids. Assessment of historical and current drinking water quality is being made in cooperation with the Environmental Protection Agency.

Identifying number: N01 CB 84229
Principal investigator: Marvin A. Kirschner
Institution: Newark-Beth Israel Medical Center
Title: Interrelationships Among Diet, Steroid Hormone Metabolism, and Human Breast Cancer

Total FY79 obligation: $132,900
Nutrition allotment: 100%
Nutrition Funding: $132,900

Total FY80 obligation: $131,400
Nutrition allotment: 100%
Nutrition funding: $131,400

Project description:

This project is to study the metabolism of steroid hormones as influenced by diet, i.e., rates of hormone production, secretion, and metabolism in relation to dietary changes. The study will, specifically, examine in-depth steroid hormone production, metabolism, and excretion in a cohort of obese American women undergoing drastic weight reduction and diet manipulation. Values obtained will be compared to those of a lean, age-matched group of normal women serving as controls. In the dietary regimens, attention will be paid to components such as fat, cholesterol, and animal protein.

These women will be examined for 1) androgen, estrogen, and cortisol production rates; 2) interconversion rates of androgens to estrogens; and 3) peripheral metabolism of androgens, estrogens, and cortisol to their usual urinary metabolites as well as alternate metabolites of the 6-beta-hydroxy series.

Identifying number: N01 CB 84238
Principal investigator: Gary D. Friedman
Institution: Kaiser Foundation Research Institute
Title: Lipid Levels and Cholesterol Metabolism in Relation to Human Breast Cancer Risk

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project is to explore a possible etiologic role of lipid(s) in breast cancer by examination of breast cancer incidence in relation to previous serum levels of cholesterol and lipids. This 1-year study will use data from the Northern California Kaiser Health Plan multiphasic health checkups on 95,000 women between 1964 and 1972. It is expected that data on more than 250 breast cancer patients will be available for review. Medical data on cholesterol and, for some subjects, on lipid levels will be available for periods well before the diagnosis of cancer. Epidemiologic data will be collected for all patients on known and suspected risk factors for breast cancer. These data will be analyzed for possible relationships between cholesterol levels and other possible etiologic factors in breast cancer and will consider, in particular, potential confounding variables such as obesity and ethnic background. Available information on indirect indicators of nutritional status will be included in the data collected. The completeness of followup will be assessed and the analysis will allow for possible sources of error due to inaccessibility of some subjects to followup.

Identifying number: N01 CB 84317
Principal investigator: Millicent W. Higgins
Institution: University of Michigan
Title: Prospective Study of Breast Cancer in Tecumseh Women

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project will explore a possible etiologic role of lipids and cholesterol in breast cancer by examination of breast cancer incidence in relation to previous serum levels of cholesterol and triglycerides. This will be an 18-month study that will use data from the Tecumseh, Michigan, study on heart disease and circulatory and respiratory diseases (an ongoing project that has studied members of this community since 1959; cholesterol and triglyceride levels as well as other details of medical history are on record). All cases of breast cancer to date will be identified and the diagnosis confirmed; it is estimated that about 60 cases of breast cancer will be identified by the end of followup for the present study.

Identifying number: N01 CB 84318
Principal investigator: Angelos E. Papatestas
Institution: Mount Sinai Medical Center
Title: Diet and Cholesterol Metabolism in Breast Cancer

Total FY79 obligation: $212,000
Nutrition allotment: 100%
Nutrition funding: $212,000

Total FY80 obligation: $225,200
Nutrition allotment: 100%
Nutrition funding: $225,200

Project description:

The goal of this project is to explore the role of lipids in breast cancer to evaluate whether dietary or metabolic factors affect causal mechanisms for the development of breast cancer systemically or locally at the target organ. This will be a pair-wise matched case-control study. Matching criteria are age, race, and menopausal status. Data on past medical and family history, dietary habits, lipid levels and cholesterol metabolism in patients with breast cancer and in controls (patients and volunteers) will be analyzed. Correlations between these parameters and epidemiological risk factors or tumor characteristics will be examined. Data on tissue enzymes, fat cell size, and hormone receptors will be examined for correlations with lipid levels.

Identifying number: N01 CN 85392
Principal investigator: John A. Hackley
Institution: Hillhaven Hospice, Tacoma, Washington
Title: Implementation of Hospice Concept for Terminal Cancer Patients

Total FY79 obligation: $450,000
Nutrition allotment: 1%
Nutrition funding: $4,500

Total FY80 obligation: $214,808
Nutrition allotment: 1%
Nutrition funding: $2,148

Project description:

A limited demonstration program will be implemented to field test in the United States the St. Christopher's Hospice concept for care of the terminal cancer patient. The hospice program will consist of two major components: a large home care program admitting a minimum of 150 patients annually and a 34-bed inpatient facility.

Identifying number: N01 CO 85409
Principal investigator: David J. Chivers
Institution: University of Cambridge
Title: Development of a Primate Research Program in Malaysia

Total FY79 obligation: $62,000
Nutrition allotment: 10%
Nutrition funding: $6,200

Total FY80 obligation: $320,226
Nutrition allotment: 10%
Nutrition funding: $32,022

Development of a Primate Research Program in Malaysia (continued)

Project description:

Coordination services will be provided in the development of field and laboratory research projects on primates in Malaysia with special emphasis on preserving viable populations of each species in their natural habitat and conserving populations of each species in disturbed habitats.

Identifying number: N01 CP 85601
Principal investigator: Donald J. Mangold
Institution: Southwest Research Institute
Title: Retinoids for Laboratory Diets

Total FY79 obligation: $128,974
Nutrition allotment: 100%
Nutrition funding: $128,974

Total FY80 obligation: $46,800
Nutrition allotment: 100%
Nutrition funding: $46,800

Project description:

The goal of this study is to develop microsphere and microencapsulation formulations and procedures to stabilize NCI-provided synthetic retinoids while maintaining good bioavailability. Stability of the neat and encapsulated retinoids will be determined at 23, 37, and 45°C under various conditions. Bioavailability studies will be done on the neat and selected samples of the encapsulated retinoids with the use of rats as the animal model. The plan is to encapsulate, prove bioavailability, and furnish at least 30 experimental retinoids of either kilogram quantities per retinoid or 10-50 grams per retinoid.

Identifying number: N01 CP 85602
Principal investigator: P. P. Nair
Institution: Sinai Hospital of Baltimore
Title: Dietary Patterns and Cancer of American Vegetarians

Total FY79 obligation: $200,000
Nutrition allotment: 100%
Nutrition funding: $200,000

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project will evaluate the effect of diet and nutrition on cancer incidence among vegetarians. Dietary patterns and nutrient intake of specified vegetarian groups will be assessed; the differences in dietary patterns and nutrient intake between vegetarians and nonvegetarians will be determined; and hypotheses concerning the dietary, metabolic, and nutritional consequences of a vegetarian diet will be developed as it relates to cancer incidence. The subcontracting institutions, under the direction of the contractor, will select appropriate study populations and collect data on dietary intake.

Dietary analyses and comparisons will be performed in order to relate the effect of vegetarian diets to cancer incidence. Nutritional data on populations in the United States and India will be analyzed chemically as well as on a standardized system used by DNCP contractors. The contractor will be responsible for coding data according to a standard format.

Identifying number: N01 CP 85604
Principal investigator: Silvio Garattini
Institution: Mario Negri Institute for Pharmacologic Research
Title: Evaluation of Agents for Treating Anorexia in Cancer

Total FY79 obligation: $107,646
Nutrition allotment: 100%
Nutrition funding: $107,646

Total FY80 obligation: $64,472
Nutrition allotment: 100%
Nutrition funding: $64,472

Project description:

The purpose of this study is to explore the feasibility of developing pharmacologic agents to counteract the anorexia and cachexia of cancer in animal models. The exploration will be developed in three main stages. Literature on anorexia and cachexia associated with cancers and cancer treatments will be reviewed. Two or more animal models of the anorexia and cachexia that occur in humans with cancer will be developed and tested. The models will be used to test potential therapeutic agents for positive effects on food intake and nutritional status.

Identifying number: N01 CP 85615
Principal investigator: Elliot Denine
Institution: Southern Research Institute
Title: Studies on Toxicology of Retinoids

Total FY79 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Total FY80 obligation: $278,095
Nutrition allotment: 100%
Nutrition funding: $278,095

Project description:

Services including material, equipment, and facilities not otherwise provided by the government will be supplied as needed, to conduct acute (single dose) retinoid toxicity studies in mice at a level of five retinoids per year; make acute (single dose) retinoid toxicity studies in rats on the then retinoid compounds; and conduct 21-day toxicity studies in both rats and mice on these compounds. In these toxicity studies, both oral and intraperitoneal routes of administration will be employed. In addition, subacute 12-week studies of retinoid toxicity will be done on the retinoid compounds. These subacute studies shall employ the oral route of administration only. Endpoints for evaluation of retinoid toxicity will include x-ray determination of the frequency and number of fractured extremities, determination of hematological parameters, and chemical evaluations on blood plasma obtained from both rats and mice. Histopathological evaluations will be made on both species of animals in the 21-day and 12-week studies.

Identifying number: N01 CP 85616
Principal investigator: Fulmer Shealy
Institution: Southern Research Institute
Title: Synthesis of Retinoids for Long-Term Animal Studies

Total FY79 obligation: $332,006
Nutrition allotment: 100%
Nutrition funding: $332,006

Total FY80 obligation: $352,681
Nutrition allotment: 100%
Nutrition funding: $352,681

Project description:

The specific retinoids to be synthesized will be determined by NCI. Retinoids of the following types will be required: amide derivatives of all-*trans* retinoic acid; ether derivatives of all-*trans* retinol;

retinylidene diketones, such as retinylidene aceylacetone; and the respective 13-cis-analogs of the above. Additional new retinoids that are synthesized and evaluated in other projects of the Carcinogenesis Program will be considered for synthesis at the kilogram level under this project.

Identifying number: N01 CP 85618
Principal investigator: R. E. Herron
Institution: Texas Institute for Rehabilitation and Research
Title: Biostereometric Assessment of Nutritional Status

Total FY79 obligation: $90,733
Nutrition allotment: 100%
Nutrition funding: $90,733

Total FY80 obligation: $13,000
Nutrition allotment: 100%
Nutrition funding: $13,000

Project description:

Determination will be made with the use of biostereometrics of the body surface area, volume, and density of adult and pediatric normals and cancer patients with and without nutritional support before, during, and after treatment for their disease. Clinical and nutritional status of these individuals will also be determined at the same point in time. Biostereometric data will be correlated with clinical and nutritional data.

Identifying number: N01 CP 85620
Principal investigator: John H. Peters
Institution: SRI International
Title: Effects of Diet on Carcinogenic Potential of Secretions

Total FY79 obligation: $185,861
Nutrition allotment: 100%
Nutrition funding: $185,861

Total FY80 obligation: $243,252
Nutrition allotment: 100%
Nutrition funding: $243,252

Project description:

The purpose of this project is to develop and refine techniques for determining the mutagenic potential of various foods and of the body fluids and excretions of subjects consuming these foods. The project will identify, separate, and quantitate the compounds responsible for the mutagenic activity. Recommendations will be submitted on standardized methodologies and techniques for performing the above tasks. In addition, the applicability of these methodologies and techniques to large-scale screening will be assessed. Mean values and ranges will be determined for mutagenic potential of certain foods prepared in different ways and for the mutagenic potential of the body fluids and excretions of subjects consuming these foods.

Identifying number: N01 CP 85650
Principal investigator: Perry J. Kurtz
Institution: Battelle Memorial Institute
Title: The Toxicology of Retinoids

Total FY79 obligation: N/A

Total FY80 obligation: $271,406
Nutrition allotment: 100%
Nutrition funding: $271,406

Project description:

Conduct acute toxicity studies on retinoids in rats and mice using both oral and intraperitoneal (IP) route exposure. Conduct repeated dose toxicity studies in rats and mice for 28-day periods with daily administration of retinoids by both IP and oral routes. As part of the studies in item 2 above, conduct hematological and chemical analysis in highest dose groups showing at least 50 percent survival and in control groups using both sexes and animals treated by each route of exposure. Conduct histopathological examinations on tissues from high and control animals in both sexes, species, and routes. Preserve tissues from remaining animals in 28-day studies for subsequent examinations should such examinations be required. Conduct gross necropsies on all animals in 28-day repeated dose studies.

Identifying number: N01 CP 85651
Principal investigator: Steven Heymsfield
Institution: Emory University
Title: Protein-Calorie Undernutrition in Cancer Patients

Total FY79 obligation: $215,152
Nutrition allotment: 100%
Nutrition funding: $215,152

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to develop accurate, feasible non-invasive methods of known precision to measure the adipose, skeletal muscular, cardiac muscular, and visceral components of protein-calorie undernutrition.

Identifying number: N01 CP 85652
Principal investigator: Jere D. Haas
Institution: Cornell University
Title: Ultrasonic Assessment of Nutritional Status

Total FY79 obligation: $60,220
Nutrition allotment: 100%
Nutrition funding: $60,220

Total FY80 obligation: $16,071
Nutrition allotment: 100%
Nutrition funding: $16,071

Project description:

This project includes the development, testing, and validation of procedures for ultrasonic measurement in humans and the development of protocols for clinical investigations.

Identifying number: N01 CP 85653
Principal investigator: Philip G. Holtzapple
Institution: Upstate Medical Center
Title: Determination of Body Composition by Ultrasound

Total FY79 obligation: $197,062
Nutrition allotment: 100%
Nutrition funding: $197,062

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project includes the development, testing, and validation of procedures for the use of ultrasonic measurement in humans and the development of protocols for clinical investigation.

Identifying number: N01 CP 85654
Principal investigator: James Mullen
Institution: University of Pennsylvania
Title: Whole-Body Impedance to Predict Total Body Water

Total FY79 obligation: $71,629
Nutrition allotment: 100%
Nutrition funding: $71,629

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The purpose of this project is to determine the utility of whole-body impedance measures in estimating total body water and extracellular fluid volume.

Identifying number: N01 CP 85655
Principal investigator: Jan Van Eys
Institution: University of Texas System Cancer Center
Title: Nutritional Assessment of the Child With Cancer

Total FY79 obligation: $265,765
Nutrition allotment: 100%
Nutrition funding: $265,765

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project will evaluate and validate immunological techniques for assessing the nutritional status of children with and without cancer in the field and in clinical settings. This project will be coordinated with other DNCP projects.

Identifying number: N01 CP 85656
Principal investigator: John P. Grant
Institution: Duke University
Title: Nutritional Parameters in Cancer Patients

Total FY79 obligation: $236,650
Nutrition allotment: 100%
Nutrition funding: $236,650

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project will determine critical nutritional assessment parameters in patients with malignant diseases that can be related to the degree of malnutrition as well as impaired organ function and, subsequently, to increased morbidity and mortality. Secondly, once these critical nutritional assessment parameters have been defined, it will be the objective of this study to monitor changes in these parameters, specifically, improvement in organ function with the institution of intensive nutritional support.

Identifying number: N01 CP 85657
Principal investigator: Lloyd Axelrod
Institution: Massachusetts General Hospital
Title: Contribution of Fat Loss to Weight Loss in Patients With Cancer

Total FY79 obligation: $183,987
Nutrition allotment: 100%
Nutrition funding: $183,987

Contribution of Fat Loss to Weight Loss in Patients With Cancer (continued)

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project will evaluate and validate the use of common metabolic techniques for the study of lipolysis, such as analysis of plasma free fatty acids, glycerol, ketones, and hormones in evaluating the nutritional status of cancer patients.

Identifying number: N01 CP 85658
Principal investigator: James Mullen
Institution: University of Pennsylvania
Title: Changes in Body Composition in Cancer Patients

Total FY79 obligation: $293,266
Nutrition allotment: 100%
Nutrition funding: $293,266

Total FY80 obligation: $115,205
Nutrition allotment: 100%
Nutrition funding: $115,205

Project description:

The purpose of this project is to determine whether existing techniques for measuring body composition can be used to define body composition changes in cancer patients with specific tumor type. Standardized procedures will be used to collect data on how body composition changes occur in cancer patients before and during treatment.

Identifying number: N01 CP 85659
Principal investigator: Bandaru S. Reddy
Institution: American Health Foundation
Title: Studies of Natural Inhibitors of Chemical Carcinogens

Total FY79 obligation: $158,008
Nutrition allotment: 100%
Nutrition funding: $158,008

Total FY80 obligation: $163,336
Nutrition allotment: 100%
Nutrition funding: $163,336

Project description:

Naturally occurring nontoxic materials suitable for addition to normal diets in order to inhibit the development of large bowel and breast cancer will be identified. Specifically, the effects of a variety of dietary fibers on chemically induced colon and breast carcinogenesis in animal models will be assessed.

Identifying number: N01 CP 85660
Principal investigator: Russell O. Sinnhuber
Institution: Oregon State University
Title: Studies of Natural Inhibitors of Chemical Carcinogens

Total FY79 obligation: $43,151
Nutrition allotment: 100%
Nutrition funding: $43,151

Total FY80 obligation: $45,312
Nutrition allotment: 100%
Nutrition funding: $45,312

Project description:

Natural inhibitors of chemical carcinogens will be studied.

Identifying number: N01 CP 85662
Principal investigator: Barry Commoner
Institution: Washington University
Title: Effect of Diet on Carcinogenic Potential of Secretions

Total FY79 obligation: $131,191
Nutrition allotment: 100%
Nutrition funding: $131,191

Total FY80 obligation: $122,745
Nutrition allotment: 100%
Nutrition funding: $122,745

Effect of Diet on Carcinogenic Potential of Secretions (continued)

Project description:

The purpose of this project is to develop and refine techniques for determining the mutagenic potential of various foods and of the body fluids and excretions of subjects consuming these foods.

Identifying number: N01 CP 85663
Principal investigator: James C. Price
Institution: University of Georgia
Title: Encapsulation of Retinoids for Laboratory Diets

Total FY79 obligation: $71,396
Nutrition allotment: 100%
Nutrition funding: $71,396

Total FY80 obligation: $36,200
Nutrition allotment: 100%
Nutrition funding: $36,200

Project description:

Encapsulation procedures will be developed for retinoid compounds with the use of the three-phase suspension method and gelatin as the encapsulation agent. Bioavailability studies of retinoid compounds will be performed to obtain means and individual plasma level-time profiles after a single oral dose of each retinoid.

Identifying number: N01 CP 85674
Principal investigator: Parviz M. Pour
Institution: University of Nebraska Medical Center
Title: Prevention of Pancreatic Cancer in Animals by Retinoids

Total FY79 obligation: $135,250
Nutrition allotment: 100%
Nutrition funding: $135,250

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

The N-Nitrosobis(2-oxopropyl) amine (BOP) hamster model will be used for pancreatic carcinogenesis in retinoid inhibition studies of the carcinogenic process. In these efforts, two dose levels of carcinogens (BOP) will be used, which will result in different tumor incidences. Anticarcinogenesis studies will be conducted on at least four retinoids. Animals will be observed in initial studies for life to determine incidence, localization, size, and type of lesion for each experimental group histopathologically. As may be indicated, the animals will be killed and serial studies conducted to define mode of retinoid action as to arrest, regression, delay, or other modification. Standard laboratory hamster chow diet will be given in initial series of experiments. Analytical procedures will be followed as proposed for serum glutonic pyruvate transferase and for determination of retinoids in diets. Chemical and histopathological data will be collected according to accepted biostatistical procedures.

Identifying number: N01 CP 85675
Principal investigator: Daniel S. Longnecker
Institution: Dartmouth College
Title: Prevention of Pancreatic Cancer in Animals by Retinoids

Total FY79 obligation: $197,402
Nutrition allotment: 100%
Nutrition funding: $197,402

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project is to induce an incidence of carcinomas or preneoplastic epithelial lesions in pancreas of azerine-treated rats and N-nitrosobis(2-oxopropyl) amine-treated hamsters, and then to see if there is a decrease in the incidence, size, or number of such cancers or preneoplastic lesions among the rats and hamsters given retinoid-supplemented diets during the latent period of carcinogenesis.

Identifying number: N01 CP 91021
Principal investigator: Leonard M. Schuman
Institution: University of Minnesota
Title: Cancer Mortality Studies

Total FY79 obligation: $105,201
Nutrition allotment: 100%
Nutrition funding: $105,201

Total FY80 obligation: $124,122
Nutrition allotment: 100%
Nutrition funding: $124,122

Project description:

This is the migrant part of the Norwegian migrant studies. Case-control studies have been conducted of gastrointestinal cancers among persons of Norwegian descent in Minnesota, and a cohort of approximately 20,000 people is being monitored. In the two countries combined, nearly 40,000 persons responded to the mailed dietary questionnaire. Early results from Minnesota and Norway indicated that total vegetable intake and an index for vitamin C are negatively associated with stomach cancer. This relationship appears to be strongest among younger patients and women. Frequent use of cooked cereals among stomach cancer patients has also been noted. These studies suggest that frequent use of salted fish may be associated with an increased risk of stomach cancer in Norway. It has been suggested that changes in food preservation such as refrigeration may influence the prevention of this disease.

With respect to colorectal cancers, the situation is less clear. There is agreement that high-vegetable diets may be beneficial, whereas meat intake data may not agree with other noted studies. It appears that there may be no effect on colorectal cancer related to beef intake, but a positive association may be found with processed meats, such as sausage.

Identifying number: N01 CP 91023
Principal investigator: Pelayo Correa
Institution: Louisiana State University Medical Center, New Orleans
Title: Case Study of Cancer in Southern Louisiana

Total FY79 obligation: $184,440
Nutrition allotment: 20%
Nutrition funding: $37,000

Total FY80 obligation: $61,500
Nutrition allotment: 20%
Nutrition funding: $12,300

Project description:

This case-control study will examine lung, pancreas, and stomach cancer in southern Louisiana. Among the factors which will be studied are food, water, and caloric intake. Other issues include occupational exposure, residence, and smoking.

Identifying number: N01 CP 91043
Principal investigator: Erek Bjelke
Institution: University of Bergen
Title: Cancer Mortality Studies

Total FY79 Funds: $82,186
Nutrition allotment: 100%
Nutrition funding: $82,186

Total FY80 obligation: $81,963
Nutrition allotment: 100%
Nutrition funding: $81,963

Project description:

This project in Norway is the basic part of the Norwegian migrant study conducted in collaboration with Dr. Schuman at the University of Minnesota. In the two countries combined, 40,000 persons responded to the mailed dietary questionnaire. Early results from Minnesota and Norway indicated that total vegetable intake and an index for vitamin C are negatively associated with stomach cancer. This relationship appears to be strongest among younger patients and women. Frequent use of cooked cereals among stomach cancer patients has also been noted. These studies suggest that frequent use of salted fish may be associated with an increased risk of stomach cancer in Norway. It has been suggested that changes in food preservation such as refrigeration may influence the prevention of this disease.

With respect to colorectal cancers, the situation is less clear. There is agreement that high-vegetable diets may be beneficial, whereas meet intake data may not agree with other noted studies. It appears that there may be no effect on colorectal cancer related to beef intake, but a possible association may be found with processed meats, such as sausage.

Identifying number: N01 CB 94327
Principal investigator: Richard A. Ahrens
Institution: University of Maryland, College Park Campus
Title: Development of Cancer Cachexia Hypophagia

Total FY79 obligation: $34,983
Nutrition allotment: 100%
Nutrition funding: $34,983

Total FY80 obligation: $38,703
Nutrition allotment: 100%
Nutrition funding: $38,703

Project description:

The project is to investigate the separate and interactive effects of exercise and variation in dietary carbohydrate source on the systemic response of rats to growth of tumors, with particular reference to food intake, carcass depletion (cachexia), and blood lactate.

Identifying number: N01 CP 95603
Principal investigator: Jon L. Spargur
Institution: Capital Systems Group, Inc., Rockville, Maryland
Title: Support to the Diet, Nutrition and Cancer Program

Total FY79 obligation: $763,701
Nutrition allotment: 100%
Nutrition funding: $763,701

Total FY80 obligation: $500,000
Nutrition allotment: 100%
Nutrition funding: $500,000

Project description:

Technical and managerial support will be provided to the DNCP including planning and preparing program, technical, and scientific documents; maintaining liaison with individuals and organizations involved and interested in the DNCP; developing and preparing information materials and handbooks for professionals; assisting with workshops, conferences, and symposia; providing support for budget and planning; and providing statistical analysis, data processing, data coordinating, and logistical support as required.

Identifying number: N01 CP 95604
Principal investigator: John H. Weisburger
Institution: American Health Foundation
Title: Colon Carcinogenesis

Total FY79 obligation: $81,217
Nutrition allotment: 100%
Nutrition funding: $81,217

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project is to conduct studies in carcinogenesis of the colon. Studies will be done on the effect of high dietary fat on DMBA-induced colon and breast carcinogenesis in germfree and conventional rats and on the effect of high-density fat on MNU-induced colon carcinogenesis in germfree and conventional female rats. The inhibitory effect of vitamin C on DMBA- or MNU-induced colon carcinogenesis will be studied in conventional female rats.

Identifying number: N01 CP 95605
Principal investigator: Lee J. Wilkoff
Institution: Southern Research Institute
Title: Organ Culture Assay of Vitamin A Analogs

Total FY79 obligation: $110,000
Nutrition allotment: 100%
Nutrition funding: $110,000

Total FY80 obligation: Active, not funded
Nutrition allotment: 100%
Nutrition funding: None

Project description:

This project is to perform an organ culture assay of vitamin A analogs.

Identifying number: N01 CM 97267
Principal investigator: Ronald Feld
Institution: Ontario Cancer Institute
Title: Nutrition as Adjunct to Chemotherapy in Lung Cancer

Total FY79 obligation: $552,925
Nutrition allotment: 100%
Nutrition funding: $552,925

Total FY80 obligation: $141,035
Nutrition allotment: 100%
Nutrition funding: $141,035

Project description:

This study will determine how nutritional support given during chemotherapy affects tumor response and patient survival in patients with advanced small-cell anaplastic carcinoma of the lung.

Identifying number: N01 CM 97268
Principal investigator: Charles G. Moertel
Institution: Mayo Foundation
Title: Phase II Studies in Gastrointestinal Cancer

Total FY79 obligation: $203,107
Nutrition allotment: 10%
Nutrition funding: $20,311

Total FY80 obligation: $213,715
Nutrition allotment: 10%
Nutrition funding: $21,372

Project description:

Studies will be done on a minimum of 40 patients per year with either pancreatic or gastric cancer and an additional 40 patients with colorectal cancer. Protocols specify nutritional assessment, i.e., caloric intake and nutritional support. Nutritional status will be studied with the use of body weight as a prognostic indicator.

Identifying number: N01 CM 97310
Principal investigator: Philip S. Schein
Institution: Georgetown University
Title: Phase II Studies in Gastrointestinal Cancer

Total FY79 obligation: $120,000
Nutrition allotment: 10%
Nutrition funding: $12,000

Total FY80 obligation: $128,055
Nutrition allotment: 10%
Nutrition funding: $12,805

Project description:

Phase II studies on gastrointestinal cancer are under way. Protocols specify nutritional assessment, i.e., caloric intake, and nutritional support. Nutritional status will be studied with the use of body weight as a prognostic indicator.

Identifying number: N01 CM 97318
Principal investigator: Edgar Moran
Institution: University of California, Irvine
Title: Nutrition as Adjunct to Chemotherapy in Lung Cancer

Total FY79 obligation: $56,433
Nutrition allotment: 100%
Nutrition funding: $56,433

Total FY80 obligation: $60,715
Nutrition allotment: 100%
Nutrition funding: $60,715

Project description:

This study will determine how nutritional support given during chemotherapy affects tumor response and patient survival in patients with advanced small-cell anaplastic carcinoma of the lung.

Indentifying number: N01 CM 97319
Principal investigator: Gerald Clamon
Institution: University of Iowa
Title: Nutrition as Adjunct to Chemotherapy in Lung Cancer

Total FY79 obligation: $121,280
Nutrition allotment: 100%
Nutrition funding: $121,280

Nutrition as Adjunct to Chemotherapy in Lung Cancer (continued)

Total FY80 obligation: $90,474
Nutrition allotment: 100%
Nutrition funding: $90,474

Project description:

This study will determine how nutritional support given during chemotherapy affects tumor response and patient survival in patients with advanced small-cell anaplastic carcinoma of the lung.

Identifying number: N01 CM 97320
Principal investigator: Roy S. Weiner
Institution: University of Florida
Title: Nutrition as Adjunct to Chemotherapy in Lung Cancer

Total FY79 obligation: $408,012
Nutrition allotment: 100%
Nutrition funding: $408,012

Total FY80 obligation: $128,117
Nutrition allotment: 100%
Nutrition funding: $128,117

Project description:

This study will determine how nutritional support given during chemotherapy affects tumor response and patient survival in patients with advanced small-cell anaplastic carcinoma of the lung.

Identifying number: N01 CM 97321
Principal investigator: Ronald Blum
Institution: New York University
Title: Nutrition as Adjunct to Chemotherapy in Lung Cancer

Total FY79 obligation: $99,710
Nutrition allotment: 100%
Nutrition funding: $99,710

Total FY80 obligation: $61,928
Nutrition allotment: 100%
Nutrition funding: $61,928

Project description:

This study will determine how nutritional support given during chemotherapy affects tumor response and patient survival in patients with advanced small-cell anaplastic carcinoma of the lung.

Identifying number: P30 CA 06516
Principal investigator: Emil Frei III
Institution: Sidney Farber Cancer Institute
Title: Comprehensive Cancer Center Support

Total FY79 obligation: $2,881,621
Nutrition allotment: 0.3%
Nutrition funding: $8,645

Total FY80 obligation: $2,858,333
Nutrition allotment: 0.3%
Nutrition funding: $8,574

Identifying number: P30 CA 06927
Principal investigator: Alfred G. Knudson, Jr.
Institution: Institute for Cancer Research, Philadelphia
Title: Comprehensive Cancer Center Program at Fox Chase

Total FY79 obligation: $4,270,171
Nutrition allotment: 5%
Nutrition funding: $213,509

Total FY80 obligation: $4,670,485
Nutrition allotment: 5%
Nutrition funding: $233,524

Identifying number: P30 CA 07175
Principal investigator: Henry C. Pitot
Institution: University of Wisconsin, Madison
Title: Cancer Research at the McArdle Laboratory

Total FY79 obligation: $750,565
Nutrition allotment: 3%
Nutrition funding: $22,517

Total FY80 obligation: $1,567,962
Nutrition allotment: 3%
Nutrition funding: $47,038

Identifying number: P30 CA 11198
Principal investigator: Robert A. Cooper, Jr.
Institution: University of Rochester
Title: Core Cancer Center Support

Total FY79 obligation: $1,435,081
Nutrition allotment: 1%
Nutrition funding: $14,351

Total FY80 obligation: $1,469,506
Nutrition allotment: 1%
Nutrition funding: $14,695

Identifying number: P30 CA 12227
Principal investigator: Peter N. Magee
Institution: Temple University
Title: Core Program on Carcinogenesis

Total FY79 obligation: $1,222,979
Nutrition allotment: 13%
Nutrition funding: $158,987

Total FY80 obligation: $1,321,658
Nutrition allotment: 13%
Nutrition funding: $171,815

Identifying number: P30 CA 13343
Principal investigator: Norton Nelson
Institution: New York University
Title: Research in Environmental Cancer

Total FY79 obligation: $320,990
Nutrition allotment: 16%
Nutrition funding: $51,358

Total FY80 obligation: $478,976
Nutrition allotment: 16%
Nutrition funding: $76,636

Identifying number: P30 CA 14089
Principal investigator: G. Denman Hammond
Institution: University of Southern California
Title: Comprehensive Cancer Center Core Support

Total FY79 obligation: $1,652,069
Nutrition allotment: 2%
Nutrition funding: $33,041

Total FY80 obligation: $2,311,286
Nutrition allotment: 2%
Nutrition funding: $46,226

Identifying number: P30 CA 14520
Principal investigator: Paul P. Carbone
Institution: University of Wisconsin, Madison
Title: Comprehensive Clinical Cancer Center Support

Total FY79 obligation: $1,910,901
Nutrition allotment: 8%
Nutrition funding: $152,872

Total FY80 obligation: $1,452,438
Nutrition allotment: 8%
Nutrition funding: $116,195

Identifying number: P30 CA 14626
Principal investigator: John F. Potter
Institution: Georgetown University
Title: Support for Lombardi Cancer Research Center

Total FY79 obligation: $390,487
Nutrition allotment: 2%
Nutrition funding: $7,810

Total FY80 obligation: $740,733
Nutrition allotment: 2%
Nutrition funding: $14,815

Identifying number: P30 CA 14718
Principal investigator: Jack E. White
Institution: Howard University
Title: Comprehensive Cancer Center Support

Total FY79 obligation: $59,063
Nutrition allotment: 3%
Nutrition funding: $1,772

Total FY80 obligation: $335,313
Nutrition allotment: 3%
Nutrition funding: $10,059

Identifying number: P30 CA 15655
Principal investigator: Lawrence H. Piette
Institution: University of Hawaii, Manoa
Title: Cancer Center Support

Total FY79 obligation: $474,147
Nutrition allotment: 7%
Nutrition funding: $33,190

Total FY80 obligation: $524,850
Nutrition allotment: 7%
Nutrition funding: $36,740

Identifying number: P30 CA 15704
Principal investigator: William B. Hutchinson
Institution: Hutchinson Cancer Research Center
Title: Cancer Center Support

Total FY79 obligation: $2,426,929
Nutrition allotment: 20%
Nutrition funding: $485,386

Total FY80 obligation: $3,119,217
Nutrition allotment: 2%
Nutrition funding: $62,384

Identifying number: P30 CA 16058
Principal investigator: David S. Yohn
Institution: Ohio State University
Title: Comprehensive Cancer Center Support

Total FY79 obligation: $1,447,438
Nutrition allotment: 1%
Nutrition funding: $14,774

Total FY80 obligation: $1,750,471
Nutrition allotment: 1%
Nutrition funding: $17,505

Identifying number: P30 CA 16059
Principal investigator: Walter Lawrence, Jr.
Institution: Virginia Commonwealth University
Title: Cooperative Cancer Center Core Support

Total FY79 obligation: $429,703
Nutrition allotment: 20%
Nutrition funding: $85,941

Total FY80 obligation: $391,176
Nutrition allotment: 20%
Nutrition funding: $78,235

Identifying number: P30 CA 16217
Principal investigator: Heschel J. Raskas
Institution: Washington University
Title: Cancer Center Support

Total FY79 obligation: $562,758
Nutrition allotment: 10%
Nutrition funding: $56,276

Total FY80 obligation: $612,950
Nutrition allotment: 10%
Nutrition funding: $61,295

Identifying number: P30 CA 16255
Principal investigator: Charles M. Huguley, Jr.
Institution: Emory University
Title: Cancer Center Support

Total FY79 obligation: Active, not funded
Nutrition allotment: 1%
Nutrition funding: None

Total FY80 obligation: Active, not funded
Nutrition allotment: 1%
Nutrition funding: None

Identifying number: P30 CA 16518
Principal investigator: Charles L. Neely
Institution: University of Tennessee Health Sciences Center
Title: Community Cancer Center Support

Total FY79 obligation: $315,444
Nutrition allotment: 0.2%
Nutrition funding: $631

Total FY80 obligation: $335,185
Nutrition allotment: 0.2%
Nutrition funding: $670

Identifying number: P30 CA 16520
Principal investigator: Richard A. Cooper
Institution: University of Pennsylvania
Title: Cancer Center Support

Total FY79 obligation: $777,560
Nutrition allotment: 2.5%
Nutrition funding: $19,439

Total FY80 obligation: $838,948
Nutrition allotment: 2.5%
Nutrition funding: $20,974

Identifying number: P30 CA 16598
Principal investgator: Angel A. Roman-Franco
Institution: University of Puerto Rico Medical Sciences
Title: Comprehensive Cancer Center Support

Total FY79 obligation: $167,882
Nutrition allotment: 12%
Nutrition funding: $20,146

Total FY80 obligation: $646,150
Nutrition allotment: 12%
Nutrition funding: $77,538

Identifying number: P30 CA 17056
Principal investigator: Arthur Flynn
Institution: Cancer Center, Inc.
Title: Comprehensive Cancer Center Support

Total FY79 obligation: Active, not funded
Nutrition allotment: 11%
Nutrition funding: None

Total FY80 obligation: N/A Terminated

Identifying number: P30 CA 17613
Principal investigator: Ernst L. Wynder
Institution: American Health Foundation
Title: Core Cancer Center Support

Total FY79 obligation: $1,393,037
Nutrition allotment: 32%
Nutrition funding: $445,772

Total FY80 obligation: $1,650,693
Nutrition allotment: 32%
Nutrition funding: $528,222

Identifying number: P30 CA 17701
Principal investigator: John J. Costanzi
Institution: University of Texas, Galveston
Title: Specialized Cancer Center Support

Total FY79 obligation: $483,059
Nutrition allotment: 1%
Nutrition funding: $4,831

Total FY80 obligation: $481,584
Nutrition allotment: 1%
Nutrition funding: $4,816

Identifying number: P30 CA 21742
Principal investigator: Jan W. Steiner
Institution: Illinois Cancer Council
Title: Cancer Center Support

Total FY79 obligation: $350,530
Nutrition allotment: 3%
Nutrition funding: $10,516

Total FY80 obligation: $359,590
Nutrition allotment: 3%
Nutrition funding: $10,788

Identifying number: P30 CA 22435
Principal investigator: Irwin H. Krakoff
Institution: University of Vermont and State Agriculture College
Title: Cancer Center Core Support

Total FY79 obligation: $437,508
Nutrition allotment: 2%
Nutrition funding: $8,750

Total FY80 obligation: $429,706
Nutrition allotment: 2%
Nutrition funding: $8,594

Identifying number: P30 CA 23100
Principal investigator: John Mendelsohn
Institution: University of California, San Diego
Title: Specialized Cancer Center Core Support

Total FY79 obligation: $347,122
Nutrition allotment: 10%
Nutrition funding: $3,471

Total FY80 obligation: $370,534
Nutrition allotment: 1%
Nutrition funding: $3,705

Identifying number: P30 CA 23102
Principal investigator: James F. Holland
Institution: Mount Sinai School of Medicine
Title: Cancer Center Core Support

Total FY79 obligation: $592,594
Nutrition allotment: 0.5%
Nutrition funding: $2,963

Total FY80 obligation: $563,235
Nutrition allotment: 0.5%
Nutrition funding: $2,816

Identifying number: P30 CA 23776
Principal investigator: Douglas J. Marchant
Institution: Tufts-New England Medical Center
Title: Core Cancer Center Support

Total FY79 obligation: $691,692
Nutrition allotment: 8%
Nutrition funding: $55,335

Total FY80 obligation: $619,581
Nutrition allotment: 8%
Nutrition funding: $49,566

Identifying number: Y01 CP 00202
Principal investigator: Joseph F. Frino
Institution: U. S. Department of Energy - Brookhaven
Title: Chemoprevention of Epithelial Cancer by Retinoids

Total FY79 obligation: N/A

Total FY80 obligation: $162,030
Nutrition allotment: 100%
Nutrition funding: $162,030

Project description:

This project is designed to study the effect of retinyl acetate on x-ray-induced mammary gland carcinogenesis. Using a single x-ray dose and a single does of retinyl acetate, the Agency research staff intends to determine the extent to which retinyl acetate can arrest, delay, or reverse the development of mammary cancer over the lifespan of the female Sprague-Dawley rat.

Identifying number: Y01 CO 00321
Principal investigator: Richard L. Leith
Institution: U. S. Department of Energy - Brookhaven
Title: Tritum Toxicity (Tritox) Program

Total FY79 obligation: N/A

Total FY80 obligation: $145,350
Nutrition allotment: 100%
Nutrition funding: $145,350

Project description:

This contract involves the study of water contaminated with tritium, and its effects on mice, including the genetic effects on reproductive efficiency, the cytogenetic effects on liver cells, and the somatic effects on bone marrow. The Relative Biological Effectiveness (RBE) of tritium compared to cesium-137 for several biological endpoints will also be estimated.

Identifying number: Y01 CP 00500
Principal investigator: Anne P. Lanier
Institution: U. S. Centers for Disease Control
Title: Epidemiology Studies In Cancer In Alaskan Natives

Total FY79 obligation: N/A

Total FY80 obligation: $120,639
Nutrition allotment: 100%
Nutrition funding: $120,639

Project description:

The CDC shall study the incidence of cancer in Alaskan natives from 1974 onwards in conjunction with the Environmental Epidemiology Branch of the NCI. The study is designed to pick up regional differences in cancer incidence and allows researchers to document past and present morbidity/mortality trends. The approach will include an environmental questionnaire (with emphasis on diet) and screening tests to measure or identify carcinogens in the diet.

Identifying number: Y01 CP 50200
Principal investigator: R. A. Griesemer
Institution: U. S. Department of Energy-Oak Ridge National Laboratory
Title: Cocarcinogenesis Program

Total FY79 obligation: $580,693
Nutrition allotment: 8%
Nutrition funding: $46,455

Total FY80 obligation: N/A Terminated

Project description:

This interagency agreement involves multiple studies of cancer and the process of chemical carcinogenesis. The following are areas of active research: respiratory carcinogenesis, nitrosamine carcinogenesis, membrane turnover related to repair mechanisms, DNA repair, cell biology, and chemical carcinogenesis. The mechanism of action of carcinogens is included in this program.

Identifying number: Y01 CP 60505
Principal investigator: Kenneth Bridbord/Anthony Robbins
Institution: National Institute for Occupational Safety and Health
Title: Research on Occupational Carcinogenesis

Total FY79 obligation: $3,769,960
Nutrition allotment: 1%
Nutrition funding: $37,700

Total FY80 obligation: $2,848,300
Nutrition allotment: 1%
Nutrition funding: $28,483

Project description:

Occupational factors to be studied include exposure to polybrominated biphenyls found in animal feed and dairy products.

Identifying number: Y01 CP 70227
Principal investigator: Thomas J. Slaga
Institution: Energy Research and Development Administration
Title: In Vitro Transformation of Tumor-Sensitive Epidermal Cells: A Bioassay and Model for the Study of the Mechanism of Action of Tumor Initiators and Promoters

Total FY79 obligation: $353,800
Nutrition allotment: 10%
Nutrition funding: $35,380

Total FY80 obligation: $179,415
Nutrition allotment: 10%
Nutrition funding: $17,941

Projection description:

The purpose of this project is to 1) isolate epidermal cells from newborn (1-3 day old) BALB/c tumor-sensitive and tumor-resistant mice by the trypsin flotation method and culture them in both Medium 199 and Waymouth's 752/1 medium; 2) treat the primary cultures with various concentrations of chemical carcinogens including MNNG, DMBA, 3-MC, BP, BP-7, 8-diol, BP-7,8-diol-9-10-epoxide, and dibenz[a,c]anthracene; 3) test the cells starting with the secondary culture for growth, absence of microtubules, and tumorigenicity in syngeneic mice and/or nude mice; 4) isolate epidermal cells from adult (7-9 week old) mice and treat and test these cells as in 2 and 3 above; 5) determine whether analogs of L-ornithine used both in vivo and in cultures of epidermal cells can inhibit TPA-induced epidermal ODC; 6) determine if putrescine, spermidine, and spermine are tumor promotors in vivo and in vitro; and 7) study the intracellular binding of labeled TPA and determine the effects of FA and certain vitamin A analogs on TPA binding.

Identifying number: Y01 CP 80207
Principal investigator: Stanton H. Cohn/Joseph F. Frino
Institution: Department of Energy-Brookhaven
Title: In Vivo Quantification of Body Nitrogen by Whole-Body Neutron Activation

Total FY79 obligation: $412,513
Nutrition allotment: 100%
Nutrition funding: $412,513

Total FY80 obligation: $545,706
Nutrition allotment: 100%
Nutrition funding: $545,706

Project description:

This will be a coordinated multidisciplinary project which will clarify questions raised by other DNCP projects in the clinical field. This project will 1) determine the absolute levels of total body potassium (TBK) and nitrogen (TBN) in normals by whole-body counting and in vivo neutron-activation analysis, respectively; 2) determine levels of total body water (TBW) in humans by appropriate methods; 3) determine normal ranges for TBN in women and men (black and white) between the ages of 20 and 90; 4) determine the effect of cancer and cancer therapy on TBK and TBN in patients under usual hospital protocols; 5) determine whether nutritional support to cancer patients during treatment alters TBK and TBN; and 6) determine which clinical parameters are accurate predictors of TBK and TBN.

Identifying number: Y01 CP 80208
Principal investigator: Niel A. Littlefield
Institution: National Center for Toxicological Research
Title: Interactions of Diet/Nutrition and the Use of Genetically Distinct Animal Strains in Carcinogenesis Studies

Total FY79 obligation: $250,000
Nutrition allotment: 100%
Nutrition funding: $250,000

Total FY80 obligation: $113,600
Nutrition allotment: 100%
Nutrition funding: $113,600

Projection description:

This project will evaluate the effect of diet on incidence of spontaneous and/or chemically induced tumors in specific strains of mice. Two defined dietary regimes will be used in combination with specific carcinogenic agents to compare effect of a semipurified diet and a natural product diet on carcinogenesis.

A long-term chronic feeding study will be initiated to determine the effects of type of diet and estrogen level on spontaneous and estrogen-induced carcinogenesis in four types (sex x strain) of laboratory mice.

Identifying number: Y01 CP 90210
Principal investigator: R. L. Jolley
Institution: U.S. Department of Energy-Oak Ridge National Laboratory
Title: Third Water Chlorination Conference: Environmental Impact and Health Effects

Total FY79 obligation: $5,000
Nutrition allotment: 100%
Nutrition funding: $5,000

Total FY80 obligation: $5,000
Nutrition allotment: 100%
Nutrition funding: $5,000

Project description:

This is a cooperative arrangement involving the Union Carbide Corporation, the U.S. Department of Energy, and NCI. The Union Carbide Corporation will conduct conferences and workshops for scientists on various aspects of chlorination.

Identifying number: F32 CA 05651
Principal investigator: Murad Ookhtens
Institution: University of California
Title: Nutritional Control of Fat Oxidation in Cancerous Mice

Total FY79 obligation: $15,300
Nutrition allotment: 100%
Nutrition funding: $15,300

Total FY80 obligation: N/A Terminated

Project description:

This is a postdoctoral research project which involves study of the oxidation of essential and nonessential fatty acids by cancer cells in living animals. Initially, the oxidative rates of fatty acids in tumor and host tissues will be measured; this determination is essential for the further development of the multicompartmental model for fatty acid metabolism in the tumor-bearing mouse. The fellow has been trained in biomedical engineering and is obtaining additional training in biomathematics and metabolic systems under the sponsorship of an established investigator in lipid metabolism.

Identifying number: F32 CA 05853
Principal investigator: Lewis D. Yecies
Institution: Washington University
Title: Fatty Acid Metabolism in Neoplasm and Inflammation

Total FY79 obligation: $16,334
Nutrition allotment: 100%
Nutrition funding: $16,334

Total FY80 obligation: N/A Terminated

Project description:

The objective of this postdoctoral research is the purification and characterization of slow-reacting substance (SRS). SRS appears to be a generalized mediator of inflammation that is produced by various phagocytic and neoplastic cells. It has been determined that the essential fatty acid, arachidonic acid, serves as a precursor of SRS for some, but perhaps not all, these cells. The fellow has been trained in internal medicine and is preparing for a career in academic medicine upon completion of this training under the sponsorship of an established investigator in allergy and immunology.

Identifying number: F32 CA 06249
Principal investigator: Lester A. Reinke
Institution: University of North Carolina
Title: Mixed-Function Oxidation in the Etiology of Cancer

Total FY79 obligation: $14,200
Nutrition allotment: 100%
Nutrition funding: $14,200

Total FY80 obligation: N/A Terminated

Project description:

This postdoctoral research project involves the study of factors that regulate mixed-function oxidase in perfused rat liver, such as age and nutritional state, and inhibitors and stimulators of drug metabolism. These studies will provide the basis for a model of regulation of activation of precarcinogens by mixed-function oxidation in the intact cell. The fellow has been trained in pharmacology and medical sciences and is taking additional training with a sponsor who is expert in the use of the perfused liver in the study of control of mixed-function oxidation reactions.

Identifying number: T32 CA 09035
Principal investigator: Thomas F. Anderson
Institution: Sloan-Kettering Institute for Cancer Research
Title: Postdoctoral Training Program in Cancer Research

Total FY79 obligation: $238,544
Nutrition allotment: 15%
Nutrition funding: $35,782

Total FY80 obligation: $269,296
Nutrition allotment: 15%
Nutrition funding: $40,394

Project description:

One postdoctoral trainee is investigating the formation of carcinogenic complexes in hamsters after gastric administration of 3-methylcholanthrene. Another trainee is studying the effect of eating plants containing coumarin upon human albumin structure.

Identifying number: T32 CA 09112
Principal investigator: George H. Buchi
Institution: Massachusetts Institute of Technology
Title: Carcinogenesis and Drug Development

Total FY79 obligation: $254,503
Nutrition allotment: 20%
Nutrition funding: $50,800

Total FY80 obligation: $322,903
Nutrition allotment: 20%
Nutrition funding: $64,581

Project description:

Three trainees are investigating metabolites of carcinogenic polycyclic hydrocarbons and the activation of amines as carcinogens. These carcinogens are occasional dietary constituents.

Identifying number: T32 CA 09135
Principal investigator: Henry C. Pitot
Institution: University of Wisconsin
Title: Predoctoral Training in Experimental Oncology

Total FY79 obligation: $310,661
Nutrition allotment: 5%
Nutrition funding: $15,533

Total FY80 obligation: $465,502
Nutrition allotment: 5%
Nutrition funding: $23,275

Project description:

Two trainees are studying naturally occurring carcinogenic compounds in food and the promotion of carcinogenesis by dietary substances.

Identifying number: T32 CA 09175
Principal investigator: Jan W. Kuzma
Institution: Loma Linda University
Title: Graduate Training Program in Cancer Epidemiology

Total FY79 obligation: $27,258
Nutrition allotment: 100%
Nutrition funding: $27,258

Total FY80 obligation: $30,020
Nutrition allotment: 100%
Nutrition funding: $30,020

Project description:

Two trainees are investigating the relationship between the diet of Seventh-Day Adventists and cancer incidence.

Identifying number: K04 CA 00324
Principal investigator: Charles P. Burns
Institution: University of Iowa
Title: Leukemia Leukocytes, Lipids and Membrane Structure

Total FY79 obligation: $38,556
Nutrition allotment: 100%
Nutrition funding: $38,556

Total FY80 obligation: $36,532
Nutrition allotment: 100%
Nutrition funding: $36,532

Project description:

This research career development awardee has been studying the effect of the diet on leukocyte membrane lipid composition and on leukocyte lipid metabolism for L1210 leukemic mice and for normal human subjects. The object of this research is to relate lipid metabolism and composition to tumor growth kinetics during early and late stages of tumor growth and to investigate the effect of altered lipid composition of the leukocyte membrane on the efficacy of antileukemia drugs. The awardee has a solid background in both clinical and basic science and is becoming an established investigator in hematology and oncology.

Identifying number: K04 CA 00460
Principal investigator: Phyllis R. Strauss
Institution: Northeastern University
Title: Thymidine Transport in Normal and Leukemia Lymphocytes

Total FY79 obligation: $32,289
Nutrition allotment: 100%
Nutrition funding: $32,289

Total FY80 obligation: $41,548
Nutrition allotment: 100%
Nutrition funding: $41,548

Project description:

The usual teaching commitments in the biology department have been considerably lightened to allow this research career development awardee to study the mechanisms responsible for regulating the uptake of nutrients and nucleosides by normal and leukemia leukocytes. The object of these studies is to define differences between the cell types. The studies involve detailed investigations of the processes of thymidine uptake and transport by nonadherent spleen cells from normal and leukemic mice.

Identifying number: K04 CA 00526
Principal investigator: John S. Schutzbach
Institution: University of Alabama
Title: The Biosynthesis of Mammalian Glycoproteins

Total FY79 obligation: $38,670
Nutrition allotment: 100%
Nutrition funding: $38,670

Total FY80 obligation: $42,120
Nutrition allotment: 100%
Nutrition funding: $42,120

Project description:

Research will be conducted on the biosynthesis of mammalian glycoproteins.

Identifying number: K04 CA 00628
Principal investigator: Sheldon M. Schuster
Institution: University of Nebraska
Title: Asparagine Biosynthesis in Normal and Tumor Cells

Total FY79 obligation: $27,745
Nutrition allotment: 100%
Nutrition funding: $27,745

Total FY80 obligation: $36,826
Nutrition allotment: 100%
Nutrition funding: $36,826

Project description:

Teaching obligations in the chemistry department have been reduced almost 90 percent to permit this research career development awardee to carry out research aimed at a chemical definition of the mechanisms by which normal and tumor cells control the synthesis of asparagine. One part of the study involves characterization of dietary effects on the distribution of two forms of asparagine synthetase. This research is aimed at increasing our understanding of asparagine-dependent and independent tumor cells.

Identifying number: K04 CA 00629
Principal investigator: Ann W. Sorenson
Institution: University of Utah
Title: Hexosaminidase Levels and Diet

Total FY79 obligation: $29,025
Nutrition allotment: 100%
Nutrition funding: $29,025

Total FY80 obligation: N/A Terminated

Project description:

This research career development award will enable this nutritionist to develop and enhance career goals in epidemiology. A part of her studies of the epidemiology of breast cancer involves comparison and search for correlations among enzyme, dietary, and hormone varibles in the patients' controls. Potential correlations include nutrient-to-nutrient interactions, nutrient-to-hormone interactions, and determination of differences in diet and/or life style that can serve as the basis for helping persons at risk for breast cancer set new goals to decrease their risk.

Identifying number: K04 CA 00764
Principal investigator: Ann W. Sorenson
Institution: Johns Hopkins University
Title: Hexosaminidase Levels and Diet

Total FY79 obligation: N/A

Total FY80 obligation: $38,479
Nutrition allotment: 100%
Nutrition funding: $38,479

Project description:

This research career development award will enable this nutritionist to develop and enhance career goals in epidemiology. A part of her studies of the epidemiology of breast cancer involves comparison and search for correlations among enzyme, dietary, and hormone variables in the patients' controls. Potential correlations include nutrient-to-nutrient interactions, nutrient-to-hormone interactions, and determination of differences in diet and/or life style that can serve as the basis for helping persons at risk for breast cancer set new goals to decrease their risk.

Identifying number: K06 CA 03449
Principal investigator: Cyrus E. Rubin
Institution: University of Washington
Title: Human Mucosal Structure and Function

Total FY79 obligation: $25,000
Nutrition allotment: 100%
Nutrition funding: $25,000

Total FY80 obligation: $31,626
Nutrition allotment: 100%
Nutrition funding: $31,626

Project description:

During tenure of the research career award this investigator has devoted part of his efforts to study the effects of luminal long-chain fatty acid concentrations on their absorption via the portal veins or lymphatics. It has been shown that the essential long-chain fatty acid, linolenic, in the low concentrations found in the usual meal, may be absorbed substantially via the portal vein. Future plans include characterization of those transport proteins involved in fat absorption.

Identifying number: K07 CA 00727
Principal investigator: David Schottenfeld
Institution: Memorial Hospital for Cancer and Allied Diseases
Title: Preventive Oncology Academic Award

Total FY79 obligation: N/A

Total FY80 obligation: $48,954
Nutrition allotment: 10%
Nutrition funding: $4,895

Project description:

Epidemiology provides the scientific foundation for the theory and practice of preventive medicine. The multifactorial origin and multistage evolution of many human cancers is now recognized. The contribution of cancer epidemiology is in identifying risk factors, providing clues for understanding etiologic mechanisms and developing the scientific rationale for the effective application of preventive measures. The implementation of preventive measures, the transfer of scientific technology to the decisionmaking process of regulatory agencies, and the modification of behavior are the ultimate challenges of preventive oncology.

Preventive Oncology Academic Award (continued)

Through the Preventive Oncology Academic Award Program, the applicant is seeking to strengthen and expand existing research programs and to facilitate a coordinated educational effort in preventive oncology which would encompass undergraduate medical students, post-graduate clinical housestaff, attending staff and nurse practitioners at the Memorial Sloan-Kettering Cancer Center and at Cornell University Medical College.

To accomplish this, the applicant plans to cooperate with other departments in the center including the Division of Education, the Department of Nursing, the Nutrition Service of the Department of Medicine, the Clinical Information Center, the Cancer Communication Office and others.

Identifying number: K07 CA 00730
Principal investigator: Jeanne Stellman
Institution: Columbia University
Title: Preventive Oncology Academic Award

Total FY79 obligation: N/A

Total FY80 obligation: $52,029
Nutrition allotment: 10%
Nutrition funding: $5,203

Project description:

The objectives of the proposed research are to further develop the education and training of professional personnel in preventive oncology; to develop an outreach educational program for lay and professional audiences, with a particular emphasis on occupational health and primary prevention and to develop field work practical experiences in primary prevention and areas such as occupational medicine for medical and science students. Basic research objectives include continuation of current efforts in understanding the risks associated with heavy metal exposure; determination of risk for leukenogenesis associated with ethylene oxide exposure among hospital workers; and elucidation of the toxic effect of agent orange exposure among Vietnam veterans.

Identifying number: K07 CA 00732
Principal investigator: Diane Russell
Institution: University of Arizona
Title: Preventive Oncology Academic Award

Total FY79 obligation: N/A

Total FY80 obligation: $77,887
Nutrition allotment: 75%
Nutrition funding: $58,415

Project description:

The major objective is to establish at the Arizona Health Sciences Center a strong combined basic and clinical program in cancer prevention. Research into the mechanism of inhibition of neoplastic growth by vitamin A analogs offers promise that analogs can be developed that not only can be used in cancer chemotherapy, but which may indeed decrease or prevent tumorigenesis. Clinical pharmacologists and oncologists will be recruited to receive extensive training in basic research targeted toward preventative oncology. These studies would be clinically applied as a function of the dual interest of the trainees in basic research and clinical application. The cancer center is committed to offering its educational facilities to assist in the development of this program. Attempts will be made to provide a number of informative lectures of interest to the community, which would summarize the current preventive measures which have been shown to decrease the incidence of specific cancers. This type of program could lead to the development of local support mechanisms to fund research into cancer prevention. A course in preventive oncology would be developed and offered to medical students, graduate students, and as a continuing education course for practicing oncologists.

Identifying number: Z01 OD 00001
Principal investigator: Lorraine Kershner
Institution: National Cancer Institute
Title of research: Nutrition Communications Activities

Total FY79 obligation: $21,000
Nutrition allotment: 100%
Nutrition funding: $21,000

Total FY80 obligation: N/A Terminated

Project description:

The purpose of this project is the coordination and dissemination of nutrition information.

Identifying number: Z01 CB 00944
Principal investigator: Seoras D. Morrison
Institution: National Cancer Institute
Title: Total Metabolism of Cancer Cachexia

Total FY79 obligation: $130,000
Nutrition allotment: 100%
Nutrition funding: $130,000

Total FY80 obligation: $146,250
Nutrition allotment: 100%
Nutrition funding: $146,250

Project description:

This project is directed toward identifying the causes of the nutritional depletion and general deterioration of the host, known as cancer cachexia, with a view to blocking or reversing these systemic effects of cancer, so that the cancer patient could become more accessible to anticancer therapies. The approach to this is by investigation of total energy, water, and other material exchanges, and of the physiological and behavioral control of food and water intake in normal and cancerous organisms.

Identifying number: Z01 CM 00998
Principal investigator: Eli Glatstein/John G. Schwade
Institution: National Cancer Institute
Title: Study of Radiation Sensitizers in Carcinoma of the Esophagus

Total FY79 obligation: $100,000
Nutrition allotment: 10%
Nutrition funding: $10,000

Total FY80 obligation: $135,000
Nutrition allotment: 10%
Nutrition funding: $13,500

Project description:

The purpose of this project is to study radiation-sensitizing compounds and their ability to increase the effect of radiation in sterilizing neoplastic cells. The plan is to take patients who have carcinoma of the esophagus that appears to be clinically confined to the mediastinum and give all patients preoperative irradiation. Half the patients will receive misonidazole, a hypoxic cell sensitizer, administered by an intravenous method. After completion of the radiotherapy, surgery will be performed and survival, freedom from lapse, and tumor viability within the pathologic specimen will all be evaluated. These patients, who are frequently cachetic, will serve as the basis for controlled studies of total parenteral nutrition.

Identifying number: Z01 CM 03509
Principal investigator: Richard M. Adamson
Institution: National Cancer Institute
Title: Carcinogenesis, Chemotherapy, and Biological Markers in Nonhuman Primates

Total FY79 obligation: $90,000
Nutrition allotment: 20%
Nutrition funding: $18,000

Total FY80 obligation: $135,000
Nutrition allotment: 20%
Nutrition funding: $27,000

Project description:

The carcinogenic effects of 26 substances, including antineoplastic and immunosuppressive agents, contaminants of human foodstuffs, rodent carcinogens, pesticides, and artificial sweeteners are being evaluated in four species of nonhuman primates. Nineteen of these substances have not as yet demonstrated carcinogenic activity, although some have been on test for less than 2 years. Seven of the test compounds are carcinogenic in nonhuman primates. The effects of five of the seven compounds (DENA, DPNA, 1-nitrosopiperidine, aflatoxin B_1, and MAM-acetate) were manifested primarily as hepatocarcinogenicity. In addition, 1-methyl-1-nitrosourea induced squamous cell carcinomas of

Carcinogenesis, Chemotherapy, and Biological Markers in Nonhuman Primates (continued)

the oropharynx and esophagus. The esophageal tumors in monkeys possess many clinical and morphologic similarities to human esophageal carcinoma. Long-term treatment with procarbazine resulted in an increased incidence of malignancies, approximately one-half of which were acute myelogenous leukemia. Alpha-fetoprotein has been found to be a useful marker for diagnosing and for monitoring the success of treatment of hepatocellular carcinoma in nonhuman primates. Studies on chemoprevention of cancer in nonhuman primates with the use of various nucleophiles are in progress.

Identifying number: Z01 CB 03630
Principal investigator: Gary L. Peck
Institution: National Cancer Institute
Title: Effects of Vitamin A and Analogs on Chick and Human Skin

Total FY79 obligation: $48,000
Nutrition allotment: 100%
Nutrition funding: $48,000

Total FY80 obligation: $9,000
Nutrition allotment: 100%
Nutrition funding: $9,000

Project description:

This project will morphologically and biochemically define the mechanism of action of vitamin A and its derivatives (retinoids) in altering epidermal differentiation in embryonic skin, normal skin, and in benign and malignant lesions of skin.

Chick metatarsal skin, when cultured in vitro, is stimulated to undergo mucous metaplasia by vitamin A acid. Ultrastructural analysis alone cannot determine whether a post-translational effect, a genomic effect, or an effect of vitamin A acid on the mesenchyme is the primary mechanism involved in the inhibition of keratinization and induction of epidermal mucin biosynthesis by vitamin A acid.

Identifying number: Z01 CB 03659
Principal investigator: Gary L. Peck
Institution: National Cancer Institute
Title: Therapy of Skin Cancer and Disorders of Keratinization

Total FY79 obligation: $192,000
Nutrition allotment: 100%
Nutrition funding: $192,000

Total FY80 obligation: $126,000
Nutrition allotment: 100%
Nutrition funding: $126,000

Project description:

Oral 13-*cis*-retinoic acid is effective in the treatment of skin cancer, a variety of disorders of keratinization (lamellar ichthyosis, Darier's disease, pityriasis rubra pilaris), and cystic acne. An oral synthetic aromatic derivative of retinoic acid (R0-10-9359) was similarly tested and found to be more effective and less toxic than 13-*cis*-retinoic acid in the treatment of the disorders of keratinization.

Identifying number: Z01 CM 03800
Principal investigator: S. A. Rosenberg
Institution: National Cancer Institute
Title: Surgical Consultations and Collaborative Research in Surgical Services at NIH

Total FY79 obligation: $200,000
Nutrition allotment: 20%
Nutrition funding: $40,000

Total FY80 obligation: $270,000
Nutrition allotment: 20%
Nutrition funding: $54,000

Project description:

The Surgery Branch of the National Cancer Institute provides elective consultants for patients as well as all emergency general surgical problems. Productive collaborative efforts in clinical studies have resulted from these consultations. The Clinical Center also provides nutritional support consultation services.

Identifying number: Z01 CM 03801
Principal investigator: S.A. Rosenberg
Institution: National Cancer Institute
Title: Clinical Studies in Cancer Surgery

Total FY79 obligation: $370,000
Nutrition allotment: 10%
Nutrition funding: $37,000

Total FY80 obligation: $477,000
Nutrition allotment: 10%
Nutrition funding: $47,700

Project description:

The Surgery Branch has a variety of studies to investigate innovative therapies for patients with malignant disease. The major emphasis of these studies is in the treatment of malignant melanoma, soft tissue sarcomas, osteogenic sarcomas, and rectal cancer. The major emphasis in Surgery Branch cancer therapy is in adjunctive therapy with emphasis on the use of multiple treatment modalities in addition to surgery. One study will include the use of hyperalimentation in the treatment of rhabdomyosarcoma and neuroblastoma.

Identifying number: Z01 CP 04258
Principal investigator: Haitung King
Institution: National Cancer Institute
Title: Cancer Incidence and Related Etiologic Factors

Total FY79 obligation: $181,818
Nutrition allotment: 33%
Nutrition funding: $60,000

Total FY80 obligation: $247,498
Nutrition allotment: 33%
Nutrition funding: $74,250

Project description:

Work during the past year has included the following activities: the Japan-Hawaii migrant study has begun to shed light on factors associated with high risk of stomach cancer in Japan and high risk of colon cancer in Hawaii. The application of epidemiologic methods to biochemical research is beginning to provide an understanding of factors associated with mutagenicity. Studies of trends in cancer mortality internationally reveal consistent worldwide decrease in stomach cancer.

Preliminary analysis of cancer mortality among U.S. Chinese by nativity shows evidence of increased risk of colon cancer to the level of U.S. whites, which is comparable to the findings among Japanese migrants.

Identifying number: Z01 CP 04378
Principal investigator: T. J. Mason
Institution: National Cancer Institute
Title: U.S. Cancer Mortality Survey

Total FY79 obligation: $246,667
Nutrition allotment: 15%
Nutrition funding: $37,000

Total FY80 obligation: $337,500
Nutrition allotment: 15%
Nutrition funding: $50,625

Project description:

An analysis of cancer mortality rates and levels of trihalomethanes in drinking water revealed an association between bladder cancer and a trihalomethane exposure index. This association will be evaluated as part of a larger study to examine the cancer mortality experience in the United States relative to cancer etiology. Investigations will be carried out in selected areas of the U.S. to test specific etiologic hypotheses. Included among these are studies of lung cancer in New Jersey, colon cancer in rural Nebraska, and liver cancer in southeast Texas. Correlational analyses of bladder cancer and pancreatic cancer revealed associations with urbanization for both cancer sites, and with heavy concentration of the chemical industry for bladder cancer.

Identifying number: Z01 CP 04410
Principal investigator: Joseph F. Fraumeni, Jr./W. A. Blattner
Institution: National Cancer Institute
Title: Studies of Cancer-Prone Families

Total FY79 obligation: $120,000
Nutrition allotment: 10%
Nutrition dollars: $12,000

Total FY80 obligation: $324,000
Nutrition allotment: 10%
Nutrition funding: $32,400

Studies of Cancer-Prone Families (continued)

Project description:

Butler and Colfax counties in rural Nebraska have among the highest mortality rates for colorectal cancer in the country. The occurrence of high mortality in these areas which do not have the usual demographic characteristics associated with colon and rectal cancer prompted this study. The project will identify 100 incident colorectal cancer cases from the two counties from 1970 to the present. Cases will be matched with two hospital-based controls, and the entire cohort will be intensively interviewed to evaluate the possible etiologic roles of diet, ethnicity, occupation (including job-related chemical exposures) and genetic/familial factors in the high frequency of large bowel cancer in this area.

Identifying number: Z01 CP 04484
Principal investigator: Luigi M. De Luca
Institution: National Cancer Institute
Title: Retinoid Effect on the Surface of Cultured Transformed Cells

Total FY79 obligation: $140,000
Nutrition allotment: 100%
Nutrition funding: $140,000

Total FY80 obligation: $148,500
Nutrition allotment: 100%
Nutrition funding: $148,500

Project description:

Spontaneously transformed mouse fibroblasts (BALB/c-3T 12-3 cells) reach a lower saturation density when cultured in the presence of retinol or retinoic acid. Retinoids do not influence the number of cell divisions, but only the saturation density, since cultures seeded at different cell density stop growing when they reach a density of approximately 120,000 cells/cm^2. In previous studies retinoids also caused 3T 12-3 cells to become much more adhesive to the culture dish surface and to each other: about 95 percent or more of the untreated cells were usually lifted from the dish surface by EDTA. Retinoid treatment enhanced the adhesion cells so that only about 5 percent of them were lifted in this assay. After removal of retinoids from the culture medium, saturation density and adhesion returned to control values within 48 hours.

Identifying number: Z01 CP 04494
Principal investigator: Anita B. Roberts
Institution: National Cancer Institute
Title: Metabolism and Tissue Distribution of Natural and Synthetic Retinoids

Total FY79 obligation: $38,000
Nutrition allotment: 100%
Nutrition funding: $38,000

Total FY80 obligation: $9,000
Nutrition allotment: 100%
Nutrition funding: $9,000

Project description:

The purpose of this project is to increase the understanding of the metabolism of retinoids. Such information must be obtained before a rational approach can be taken to the design of new retinoids with greater activity in the reversal of preneoplasia in epithelial tissues. The investigation is along two basic lines: 1) the study of the in vitro metabolism of retinoic acid and synthetic retinoids in subcellular systems of target tissues as compared to nontarget tissues, and 2) the study of the biochemical activation mechanisms of the synthetic retinoids.

Identifying number: Z01 CP 04501
Principal investigator: R. N. Hoover
Institution: National Cancer Institute
Title: Case-Control Studies of Selected Cancer Sites

Total FY79 obligation: $170,000
Nutrition allotment: 15%
Nutrition funding: $25,500

Total FY80 obligation: $337,500
Nutrition allotment: 15%
Nutrition funding: $50,625

Project description:

This study is an 18-month project designed principally to provide the Commissioner of Food and Drugs with an answer to the question: Does saccharin initiate or promote human bladder cancer? The study employs a population-based case-control design. All newly diagnosed carcinomas of the urinary bladder occurring during 1978 in five designated states and four metropolitan areas will be studied. It is estimated that there will be approximately 3,200 cases. In addition, 6,400 controls will be drawn as a stratified random sample of the general population.

Case-Control Studies of Selected Cancer Sites (continued)

In addition to saccharin ingestion, other exposures will be assessed: occupation, cigarette smoking, source of drinking water, coffee consumption, and intake of liquids. Assessment of historical and current drinking water quality is being made in cooperation with the Environmental Protection Agency.

Identifying number: Z01 CP 04549
Principal investigator: Michael B. Sporn
Institution: National Cancer Institute
Title: Organ Culture Studies on Tracheobronchial Epithelium

Total FY79 obligation: $80,000
Nutrition allotment: 100%
Nutrition funding: $80,000

Total FY80 obligation: $135,000
Nutrition allotment: 100%
Nutrition funding: $135,000

Project description:

The ability of vitamin A and its synthetic analogs (retinoids) to reverse a potentially premalignant lesion of tracheobronchial epithelium is being studied in organ culture. Keratinized, squamous metaplastic lesions are established in organ cultures of hamster tracheas. Addition of active retinoids causes reversal of these lesions and restoration of healthy mucociliary epithelium. With the use of this experimental system, several new retinoids have been found to be extremely active and relatively free of toxicity.

Identifying number: Z01 CP 04580
Principal investigator: L. A. Poirier
Institution: National Cancer Institute
Title: The Role of Lipotropes in Carcinogenesis

Total FY79 obligation: $160,000
Nutrition allotment: 100%
Nutrition funding: $160,000

Total FY80 obligation: $162,000
Nutrition allotment: 100%
Nutrition funding: $162,000

Project description:

The mechanisms behind the alteration of chemical carcinogenesis by the dietary lipotropes, choline, methionine, folic acid, and vitamin B_{12} have been studied. The chronic administration of diethylnitrosamine to rats led to an increased uptake of labeled precursors into hepatic lecithin, whereas the uptake of labeled precursors into phosphatidyl ethanolamine and phosphatidyl serine was unaffected. The effects of promoters on phospholipid biosynthesis are being investigated. The elevated methionine requirement of transformed liver epithelia cells appears to be the consequence of more than one biochemical abnormality. A comparative analysis is being made of the metabolism and carcinogenic activity of methionine in different species.

Identifying number: Z01 CP 04779
Principal investigator: W. J. Blot
Institution: National Cancer Institute
Title: Analytic Studies in High-Risk Areas

Total FY79 obligation: $290,000
Nutrition allotment: 15%
Nutrition funding: $43,500

Total FY80 obligation: $337,500
Nutrition allotment: 15%
Nutrition funding: $50,625

Project description:

This project includes three studies:

1) Case-control Study of Esophageal Cancer Among Black Men in Washington, D.C.:

A case-control study of esophageal cancer is being conducted among black male residents of Washington, D.C. Black men living in the District of Columbia have mortality rates for this tumor which are among the very highest in the United States. These rates are continuing to increase. In contrast, esophageal cancer is still relatively rare among D.C.'s white male residents. This situation is highly suggestive of an environmental influence peculiar to black men of the District. The aim of this epidemiologic investigation is to identify the risk factors which may be responsible for these unusual patterns.

The study involves interviewing recently diagnosed esophageal cancer cases and controls to elicit lifetime histories of alcohol and tobacco consumption, diet, residence, occupation, and information on several other suspected risk factors for this disease. The beverage history and diet history aspects comprise approximately one-third of the questionnaire.

2) Canadian Breast Cancer Study:

This study involves interviewing about 1,300 Canadian women as controls for cases already collected in northern Alberta, Canada. The interview will include a section on dietary patterns in order to determine whether there is any relationship between dietary intake and the incidence of breast cancer.

3) Bladder Cancer in Rural New England:

A case-control interview study is being conducted, involving cases of bladder cancer diagnosed over the last 5 years in certain rural areas of Vermont, New Hampshire, and Maine. These areas are unique in having significantly elevated bladder cancer mortality rates for both sexes. The interview will include information on coffee-drinking, the use of non-nutritive sweeteners, use of bracken fern in the diet, and detailed information on sources of drinking water.

Identifying number: Z01 CP 04798
Principal investigator: Luigi M. De Luca
Institution: National Cancer Institute
Title: Vitamin A in Control of Epithelial Cell Differentiation and Carcinogenesis

Total FY79 obligation: $60,000
Nutrition allotment: 100%
Nutrition funding: $60,000

Total FY80 obligation: $135,000
Nutrition allotment: 100%
Nutrition funding: $135,000

Project description:

In an in vitro mouse epidermal cell carcinogenesis system, derivatives of retinol and retinoic acid have been found to prevent the expression of neoplastic transformation induced by phorbol esters. The least active compound was found to be anhydroretinol, a retinoid with little vitamin A activity. Retinylphosphate and retinoic acid were the most active compounds. Cultured mouse epidermal cells were found to synthesize retinylphosphate and retinylphosphate-mannose. These products were characterized by their chromatographic behavior and hydrolysis in mild alkali. This treatment released anhydroretinol from the phosphorylated vitamin. Treatment of cultured epidermal cells with excess retinol (4×10^{-5} M) greatly enhanced galactose and mannose incorporation into glycoconjugates without effect on total RNA synthesis or glucose utilization.

Identifying number: Z01 CP 05051
Principal investigator: Anita B. Roberts
Institution: National Cancer Institute
Title: Isolation of a Retinoid-Sensitive Polypeptide-Transforming Factor

Total FY79 obligation: $22,000
Nutrition allotment: 100%
Nutrition funding: $22,000

Total FY80 obligation: $135,000
Nutrition allotment: 100%
Nutrition funding: $135,000

Project description:

It has been shown that retinoids can block the phenotypic cell transformation produced by a polypeptide transforming factor, sarcoma growth factor.

The purpose of this project is to isolate such transforming factors and then to investigate the mechanism whereby retinoids can interfere with their expression. The investigation will consist initially of two parts: first, isolation and purification of sarcoma growth factor from murine sarcoma virus-transformed cells in culture and from murine sarcoma virus-induced tumors in vivo, and second, isolation and characterization of polypeptide-transforming factors from carcinogen-induced tumor of epithelial tissues, such as breast and bladder, which have been shown to be responsive to retinoid therapy.

Identifying number: Z01 CP 05052
Principal investigator: C. A. Frolik
Institution: National Cancer Institute
Title: Control of Epithelial Cell Differentiation and Carcinogenesis
by Vitamin A

Total FY79 obligation: $60,000
Nutrition allotment: 100%
Nutrition funding: $60,000

Total FY80 obligation: $67,500
Nutrition allotment: 100%
Nutrition funding: $67,500

Project description:

The ultimate goal of this project is to find an agent that will reverse preneoplasia in epithelial tissue. Vitamin A and its analog retinoids are the compounds currently being investigated. Emphasis has been placed on examining the metabolic pathway of a natural retinoid, all-trans-retinoic acid, in vivo and in vitro. Retinoic acid has been shown to undergo a tissue-dependent metabolism to several more polar-compounds in a hamster tracheal organ culture system. Two of these metabolites have been identified as 4-hydroxy-retinoic acid and 4-keto-retinoic acid. A comparison of the in vivo and in vitro metabolism of all-trans versus 13-cis-retinoic acid suggests that both compounds may be sharing a common metabolic pathway that may include an isomeric form of 4-keto-retinoic acid.

A knowledge of the metabolic pathway of retinoic acid will help to decipher the biochemical mechanism of action of vitamin A in determining epithelial cell differentiation. It will also aid in designing analogs of vitamin A that will display biological activity in the reversal of preneoplasia and, at the same time, will show low toxicity in the animal.

Identifying number: Z01 CP 05053
Principal investigator: Robert Meeks
Institution: National Cancer Institute
Title: Studies on the Mechanism of Toxicity of Natural and
Synthetic Retinoids

Total FY79 obligation: $40,000
Nutrition allotment: 100%
Nutrition funding: $40,000

Total FY80 obligation: $18,000
Nutrition allotment: 100%
Nutrition funding: $18,000

Project description:

The purpose of this project is to develop an in vitro assay system that could be used for the rapid determination of the toxicity of retinoids which, in turn, could be used to gain insight into the mechanism of action of retinoid toxicity. Such information could be used to rationally develop new retinoids with increased biological activity in the reversal of preneoplastic lesions in epithelial tissue but at the same time have decreased toxicological activity.

Identifying number: Z01 CP 05054
Principal investigator: Brian Swanson
Institution: National Cancer Institute
Title: Pharmacokinetics and Metabolism of Retinoids in Rodents

Total FY79 obligation: $46,600
Nutrition allotment: 100%
Nutrition funding: $46,600

Total FY80 obligation: $14,850
Nutrition allotment: 100%
Nutrition funding: $14,850

Project description:

An extensive study on the absorption, distribution, metabolism, and excretion of a synthetic retinoid, *N*-(4-hydroxyphenyl)-all-*trans*-retinamide (HPR), will be completed. The metabolic fate and plasma clearances of other retinamides and of all-*trans*-retinoic acid will be investigated. The effect of retinoids on hexobarbital-induced sleeping times in mice will also be studied.

Identifying number: Z01 CP 05128
Principal investigator: R. A. Ziegler
Institution: National Cancer Institute
Title: Nutritional Factors in Cancer Etiology

Total FY79 obligation: N/A

Total FY80 obligation: $76,500
Nutrition allotment: 100%
Nutrition funding: $76,500

Nutritional Factors in Cancer Etiology (continued)

Project description:

Included in this project are a number of epidemiological studies on diet and cancer. Exposures being assessed in human populations include broad dietary patterns, such as diets high in fat or meat; nutritional status, such as low vitamin A or vitamin C intake; metabolic indices, such as low serum cholestrol; specific food groups, such as Brassica vegetables; food additives; cooking practices; ethnic foods; etc. Cancer being studied include those of the colon, rectum, breast, esophagus, and lung. Case-control studies have been initiated in areas with unusually high rates of presumably diet-related cancers and in communities of immigrants whose cancer rates have been changing concurrently with adoption of new lifestyles. In situations where reliable dietary or biochemical information already exists on a number of individuals, follow-up mechanisms and retrospective cohort studies have been initiated. Interviewing methods and statistical methods that would improve data collection and analysis in nutritional epidemiology are being evaluated. Data from HANES I and II are being analyzed to provide descriptive baseline information on diet variation and nutrient levels throughout the United States.

Identifying number: Z01 CP 05137
Principal investigator: Robert W. Miller
Institution: National Cancer Institute
Title: Bedside Etiologic Consultative Program

Total FY79 obligation: N/A

Total FY80 obligation: $45,000
Nutrition allotment: 15%
Nutrition funding: $6,750

Project description:

By participation of the staff at area institutions, at the bedside and in clinical conferences, rounds and oncology clinics, patients or families with unusual features are ascertained and etiologic consultations given. Comprehensive family interviews and appropriate laboratory and epidemiologic investigations are suggested or performed yielding environmental and genetic information as a means of elucidating biologic mechanisms of carcinogenesis. Collaboration with the area institutions for systematizing acquisition and storage of data pertaining to etiologic aspects and long-term complications into the pediatric oncology registries will facilitate ongoing and future evaluation of significant pathogenetic mechanisms of carcinogenesis. One of the six areas of interest will include the relationship of infantile hepatoblastoma to fetal alcohol syndrome and the possibility of transplacental carcinogenicity of alcohol.

Identifying number: Z01 CP 05141
Principal investigator: Nancy H. Colborn
Institution: National Cancer Institute
Title: Preneoplastic Progression in Epidermal Cells

Total FY79 obligation: N/A

Total FY80 obligation: $67,500
Nutrition allotment: 25%
Nutrition funding: $16,875

Project description:

The overall objective of this research is to elucidate the cellular and molecular basis of one or more stages which must occur during progression to malignancy in response to chemical carcinogens and tumor promoters. Rational approaches to prevention of one or more stages of progression is another long-term goal. Recently published or in press results from our laboratory indicate that late stage tumor promotion by phorbol esters occurs by a process involving induction of a new phenotype (vs. selection of a preexisting variant). The mechanism appears not to require mitogenic stimulation or ornithine decarboxylase induction by the promoter. Promoter-induced changes in cell surface glycoconjugate synthesis as well as chromosome and chromatid breaks and rearrangements occur and are being investigated for their role in promotion of tumor cell phenotype. Retinoids inhibit phorbol ester promotion in this system and are being used to investigate 1) required events in promotion; and 2) cancer prevention.

Identifying number: Z01 CB 05219
Principal investigator: R. A. Knazek
Institution: National Cancer Institute
Title: In Vitro Stimulation of Hormone-Dependent Mammary Tumor Regression

Total FY79 obligation: $116,000
Nutrition allotment: 50%
Nutrition funding: $58,000

Total FY80 obligation: $112,500
Nutrition allotment: 50%
Nutrition funding: $56,250

Project description:

Target tissues respond to hormones only if specific receptors are present on or within their cells. Alterations of the hormone-receptor axis may then modify the response of target tissues (i.e., hormonal-responsive mammary carcinoma) to various hormones and serve as a

In Vitro Stimulation of Hormone-Dependent Mammary Tumor Regression (continued)

means for controlling the growth and function of such tissues. It has been shown that growth hormone induces the prolactin receptor in murine liver by acting at a site distal to the induced receptor. By making mice deficient in essential fatty acids, both the intraperitoneal and mammary gland fat are markedly decreased. These deficient animals lose the normal ductal-alveolar structures within their mammary glands, an effect that can be reversed by treatment with exogenous linoleic acid. These deficient animals also have decreased numbers of prolactin receptors within their livers and are unable to induce them by hormone injections. Prostaglandins have been implicated in the maintenance and induction of the PRL receptor in vivo. These studies indicate that specific fatty acids modulate the function of prolactin receptors, probably by altering prostaglandin synthesis. Mammary tissues have also been shown to synthesize prostaglandins at rates that vary as a function of stage in the estrous cycle. Dietary fat may modify effects of hormones on the mammary gland.

Identifying number: Z01 CM 06515
Principal investigator: Charles E. Myers
Institution: National Cancer Institute
Title: Biologic Response Modification: Free Radical Defenses and Their Modification by Nutrition

Total FY79 obligation: N/A

Total FY80 obligation: $175,000
Nutrition allotment: 100%
Nutrition funding: $175,000

Project description:

Our work with adriamycin cardiac toxicity has led us to reexamine the role of endogenous free radical defenses in moderating free radical damage. Since free radical damage is a process which plays a role in such diverse phenomena as aging, ionizing radiation damage, oxygen toxicity, carcinogenesis, and drug toxicity, we have tried to structure our investigation in such a way as to yield results pertinent to this broad range of problems rather than to focus narrowly on anthracycline cardiac toxicity. Two of the defense mechanisms we will investigate are selenium-dependent glutathione and vitamin E. By altering the diet or the genetic makeup of the mice used, we can study the effect of both mechanisms that protect mammals against free radical attack and carcinogenesis.

Identifying number: Z01 CM 06653
Principal investigator: M. F. Brennan
Institution: National Cancer Institute
Title: Metabolic Studies in Tumor-Bearing Patients and Animals

Total FY79 obligation: $340,000
Nutrition allotment: 100%
Nutrition funding: $340,000

Total FY80 obligation: $450,000
Nutrition allotment: 100%
Nutrition funding: $450,000

Project description:

The Surgery Branch is engaged in assessment of the efficacy of total parenteral nutrition as a means of nutritional support of the cancer-bearing host. These studies are directed at utilizing new methodologies employing stable isotopes and labelled substrates combined with standard assessment of nitrogen balance and 3-methylhistidine excretion as determinants of host-protein preservation.

In addition, two prospective randomized studies have been initiated. Within the lab, attempts to nutritionally deprive human tissue culture cell lines of essential amino acids are continuing. The interest continues in animal models of protein depletion and methods for preservation of host tissue by animal TPN, exercise, and steroids.

Identifying number: Z01 CB 08229
Principal investigator: William R. Kidwell
Institution: National Cancer Institute
Title: Role of Dietary Lipids in Increased Incidence of Mammary Cancer

Total FY79 obligation: $15,000
Nutrition allotment: 100%
Nutrition funding: $15,000

Total FY80 obligation: $22,500
Nutrition allotment: 100%
Nutrition funding: $22,500

Project description:

Epidemological and experimental studies have implicated high dietary fat intake in the increased incidence of mammary cancer. The fact that changes in dietary intake of lipids is reflected by comparable changes in the lipid matrix of the mammary gland suggests that fatty acids may have a direct role in mammary carcinogenesis. Experimental

Role of Dietary Lipids in Increased Incidence of Mammary Cancer (continued)

systems have been established for assessing fatty acid effects of the growth of cells from normal tissue and carcinogen-induced mammary tumors of rats.

The studies show that all unsaturated fatty acids present in the gland in appreciable amounts promote cell growth. Each fatty acid has its own characteristic concentration optimum which, with normal mammary cells, correlates with the abundance of that fatty acid in the gland. Both normal and tumor cells are inhibited by saturated fatty acids. Maximum growth rate of tumor cells is obtained with oleic acid whereas normal cells grow best in the presence of linoleic or linolenic acid.

Identifying number: Z01 CM 09112
Principal investigator: William R. Grove
Institution: National Cancer Institute
Title: An Evaluation of the Effect of Chemotherapy and Oral Antibotics on Gastrointestinal Function

Total FY79 obligation: N/A

Total FY80 obligation: $26,730
Nutrition allotment: 33%
Nutrition funding: $8,910

Project description:

The objective of this study is to evaluate the effect of chemotherapy and oral antibiotics on gastrointestinal function in a population of patients with acute non-lymphocytic leukemia in remission.

Eligible patients are those patients receiving the chemotherapy combination of thioguanine and cytosine arabinoside for maintenance chemotherapy and receiving any of the following combinations of oral antibiotics for infection prevention: gentamicin and nystatin; gentamicin and vancomycin and nystatin; nalidixic acid and nystatin; trimethoprim-sulfamethoxazole and nystatin.

The following laboratory tests are performed as a baseline, repeated at the end of the chemotherapy course and again while on oral antibiotics: serum carotene, serum vitamin A, serum folic acid, serum D-xylose (2 hr.) and urine D-xylose (5 hr.).

Sixteen patients have been entered on study. Seven patients have completed the sequence of laboratory tests. Eight patients failed to complete the tests, mostly due to the need for hospitalization to receive systemic empiric antibiotics. One patient remains on study. Additional patients will be entered on the study as they begin their maintenance courses of chemotherapy. It is too early to evaluate the data.

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